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# SOME PROBLEMS IN EPILEPSY*

PRESIDENTIAL ADDRESS

WALTER TIMME, M.D.

Our third annual meeting brings us a step further along on the road we have chosen to travel, and as becomes seasoned travellers, we find that we need to discard many of the impediments which at first were thought necessary to our journey but which have since been proved to have merely bulk out of proportion to utility. As our society is pre-eminently one for research and not for the mere compilation of extant literature, even though this latter must of necessity be gathered in our bibliography, our programs must gradually be freed from all matter not truly savoring of original thought and work. The outlook seems, therefore, to be for less extensive but more intensive presentations; and so this year's offerings will be found to have, I believe, few of the characteristics of the ordinary symposiums on epilepsy. We do not feel that the entire subject must be covered in all of its aspects, but only in those on which more light or a greater approximation than heretofore to apparent truth may be had.

The very first difficulty—and there were many encountered—that confronted your program committee, was the choice of a comprehensive title for the subject before the society. The term epilepsy as it was commonly understood was immediately found to be inadequate, for while the convulsive seizure was uppermost in the mind as the concomitant of epilepsy and was the factor largely to be discussed at this year's meeting, yet it is trite to say that, in the opinion of many, some epilepsies may have no convulsions at all in the ordinary acceptance of the term. On the other hand, many convulsive seizures that seem superficially to simulate an epilepsy, such as those occurring in uremia, diabetes, tetany, and many of the other toxaemias, may possibly not be truly epileptic. And so both terms, epilepsy and convulsion, had to be introduced into our title. It is not my function to differentiate or to define, but merely to point out the problem. You will find on our program, therefore, discussions on uremic and other toxic convulsive states and possibly even an attempt at a differential diagnosis between them and the epileptic. We shall also have exceed-

* Read before the Association for Research in Nervous and Mental Diseases, December 28, 1922.

ingly important, not to say interesting, reports of the production of convulsive attacks in animals simulating the epileptic attack, by various surgical and pharmacodynamic means. Immediately occurs the thought—if surgical experimentation and pharmacodynamic assault release a mechanism in either case producing substantially the same manifestations, the approach to such a corticomotor release may possibly be along many other paths as well. Investigators are more or less in agreement that such motor release may be occasioned by various toxins, both endogenous and exogenous—witness the eclamptic and uremic seizures, wormwood and strychnin poisoning; or by infection—syphilitic, encephalitic; or through metallic poisons, lead and mercury—or through a variety of other causes— all of which are to be separated from the anatomic causes produced by various forms and sequelae of traumatic insult, tumor, and other local irritative lesions in great number. And then, apart from these two great groups of causes of the convulsive state there is added the group of so-called idiopathic epilepsy or genuine epilepsy, with a convulsive manifestation which you will hear, during these two days, compared to the convulsive seizure of the two great pathologic groups mentioned. Are the mechanisms released in the three types the same, or do they differ in essential particulars as well as in their pathogenesis? To add to the complexity, some of us believe that instead of, or indeed in addition to, the motor release in genuine epilepsy there may be a pathologic release in other domains and on other levels than the purely motor cortical. So that in the receptors of the special senses, and other "gnostic" centers, manifestations occur with attendant specific characteristics such as peculiarities of taste or smell or vision or hearing; or again with behavioristic and moral, intellectual and psychic and symbolic disturbances, seen as the so-called epileptic equivalents—a term which degrades them to a subsidiary position, and is only just as true as though we called the "fit" itself the motor equivalent of a disturbance on the higher level. Descending to the lower levels, are there not also disturbances in the basal ganglions, in the extended vagus system and even in the various segments of the cord which lead to more or less circumscribed motor and sensory symptoms that are due to a release of some mechanism perhaps similar in its origin, but different in its point of application? The motor cortical release which, by reason of its dramatic intrusion, startles our senses into its acceptance as the "whole thing" has, by virtue of this self-advertisement, for ages dominated our conception of genuine epilepsy. Is it for this reason that the comparatively smaller and less insistent gestures have escaped their true valuation? That is to say, is a muscular fibrillation, or a myoclonus, or a subjective segmental transitory pain without any demonstrable lesion, one of the forms of release produced

in genuine epilepsy when the point of low threshold is a part of the spinal cord? It is possible that some of our theses will cover this point. As for the vegetative level, now that biochemistry is beginning to assume such magnificent proportions in our medical uncomfortableness, that is the line on which—having failed in all others—we are now concentrating our attacks. If the reason for a genuine epileptic seizure—no matter on what point it is centered—is one of lowered threshold of the synaptic junction or other salient point of defense of the nervous system, then is such lowered threshold determined by a critical change in the biochemistry of the circulating fluids, or else of the neural elements? Many observations of changes in the coagulation time of the blood, in the alkiline reserve, in the organic and inorganic retained salts and split protein products, have come down to us as some of the underlying base-stones of the lowered threshold theory. As a corollary, what abnormal function of the glands of internal secretion could account possibly for such biochemical changes? One must have great optimism to face courageously these problems and to arrive at a comprehensive view of what we have termed genuine epilepsy. Your program to-day has on its rolls some such intrepid souls, and we cannot sufficiently convey to them our appreciation of their contribution to our science.

As my function is largely today an inquisitive one, as you may have noticed, may I add to some of the simple questions thus far propounded, this: If the genuine epileptic attack—no matter of what nature and focus—is due to a lowered threshold on the part of the neural elements or their structure, is such low threshold coefficient inherent in some constitutions apart from any biochemical, toxic, or other factor; so that certain individuals will respond with an attack psychic, intellectual, behavioristic, convulsive, vagal, or vegetative, or a combination of these more readily than others? If this is so, then are such individuals even without such attack (as we have been told by some observers that they are) different in their adaptability to their environment and to their problems? Is there an epileptic personality *per se,* with not only no necessity, through an attack, for diagnosis, but actually without attack? Perhaps this part of our problem will be solved for us tomorrow.

From these more or less lucid questions and expressions, one thing, I believe, stands out prominently and that is, that to call a patient "epileptic" means almost nothing in an explanatory sense—it is merely calling him a name. If my questions were all answered affirmatively we were all potential epileptics; and yet I doubt not, many of us would answer affirmatively and consider epilepsy an expression of a failure to overcome one of the difficulties that the race, in reaching for higher

and more specialized development, encounters in its upward gradient. It would, in such a sense, be a hall-mark of the non-adaptability of the unfit in this drive for the ultimate.

I have already encroachéd too long a time on your patience and on our exercises, but something still remains to be said. If a tendency to a wider, more extensive application of the term epilepsy is apparent, it becomes increasingly our duty either to take the fear and sting from the term epilepsy—for its mere individual application is fraught with as acute perils as was the mediaeval term "heresy"; or else to invent a new name to cover the situation.

Apologetically, and in fear and trembling, may I venture to suggest that while the term epilepsy be retained to apply to all the symptoms complex that are at present thought to be due to what the term epilepsy connotes, namely, "a seizure upon" the individual through extraneous causes, such as irritative lesions and drugs and toxins, yet that a new term connoting a seizure due to causes *within,* and of the biological unit *per se,* be used to cover the inadequacies and deficiencies of the mechanism of the biological unit in its selfdefense. Such a term might be "endolepsy." Following the adoption of the complementary, and to an extent the antithetic, terms "epilepsy" and "endolepsy," we would have at once a separation on a more or less rational basis, of the many conditions heretofore known by the many hyphenated expressions that fill our discussions of the subject, into two great classes. It will tend to clarification, to definiteness of picture, to less diffuseness of argument, and with a distinct end-product for our experiment and ratiocination to prove or disprove.

Gentlemen, our greetings to you on this third anniversary meeting of our association, and our thanks for the great interest and support and assistance that you have given since the inception of our organization. Your New York confreres extend you their greetings and bid you welcome.

# THE ECOLOGY OF EPILEPSY

## I. EPILEPSY IN COLONIES *

CHARLES L. DANA, M.D.

NEW YORK

Epilepsy is not only a medical problem, it is also a social and even a zoological one; and it appeals emphatically to preventive medicine, as all incurable diseases do, or should do. These points of view are included under the term Ecology, a science that deals with groups, and with the relation of these groups to the environment. It calls for a broader view than do the ordinary studies of the nature and cause of the disease.

For epilepsy has apparently a definite injurious influence on social life and economics as well as on the individuals who suffer from the disease. My aim has been to study the disease in bulk; with reference to the social effect of massed epilepsy on society, and of the units of the mass upon each other. Another line of attack is that of inquiry into the racial, geographical and social, and even evolutional conditions that have led to the development of epilepsy in man and animals. For it seems that epilepsy has existed in every human race, and probably in all vertebrate animals, since the beginning of vertebrate and human life. It is along this last line that Dr. C. B. Davenport has made investigations.

The object of this paper is an investigation of epilepsy in mass; i. e., in epileptic colonies. The inquiries bore on the relations of the colonies to the community about them, the personality of colonies of epileptics, and the effects of segregation on the epileptics themselves; whether or not the patients with epilepsy throve en masse.

In response to a questionnaire letter to the medical directors of the nine epileptic colonies in the United States, I received lengthy and carefully thought out replies from: (1) Dr. A. S. Priddy, State Colony of Virginia; (2) Dr. A. B. Bass, State Colony of Texas; (3) Dr. F. O. Butler, of Sonoma State Home of California; (4) Dr. Benjamin W. Baker, of the School for Feeble-Minded, of New Hampshire; (5) Dr. D. F. Weeks, of Village for Epileptics of New Jersey; (6) Dr. William T. Shanahan, of Craig Colony, New York.

The opinions were unanimous that the segregation of epileptics in colonies was not harmful, but economically satisfactory to the surrounding communities, and that epileptics when living together did not react badly upon each other; but were on the whole better and happier.

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* Read at the third annual meeting of the Association for Research in Nervous and Mental Diseases, New York, Dec. 27, 1922.

The special advantages in opportunities for education, occupation and treatment have been demonstrated and are familiar to all. Incidentally, there might come up the question whether eventually an epileptic infection of the community occurs, i. e., whether in time there develops more epilepsy among the people living in and about an epileptic colony. It must be, that occasional irregular intercourse takes place between the patients and outsiders.

The establishment of epileptic colonies is proved to be a successful way of dealing with the disease, but in almost all cases the directors are dissatisfied with the inadequacy of state support. There are, I should say, nowhere in the United States ideal or model colonies for epileptics as there are for mental defectives and the insane, and nearly all the directors plead for more help, better equipment and fewer mental defectives, for the mental defective is grouped with the epileptics in many states.

This epilepsy mass has certain special features that give it a kind of personality of its own. Some of the characteristics of the group are these:

1. The group is made up of individuals who are on the whole not only incurable but steadily deteriorating. It is a dying forest growing in a fertile soil. In this respect, the group differs from that of the insane, and of the feeble-minded; the former has hope of cure, the latter of improvement.

2. There is a prevalent querulousness, irritability, dislike of discipline, and of the prolonged effort which leads to manual skill and to a definite technical occupation. The special character of the chronic deteriorating epileptic gives its quality to the atmosphere of the institution.

3. There is the greatest possible range of intelligence from idiocy to cleverness, and great variation in behavior from precise rectitude to delinquency.

4. The ever present element of the convulsive seizure gives a certain atmosphere, involving anxiety, expectancy and dramatic episodes; all toned down by familiarity with the situation.

These characteristics of massed epilepsy do not conflict with the fact that the seriously epileptic are better occupied, better educated and lead a more effective and happy life than if they were in a normal community. From epileptic colonies also are coming studies which will show us, we believe, how to prevent and lessen the prevalence of the disease.

The investigations of Professor Davenport and others show, as already stated, that the convulsive seizure is present in all levels of vertebrate life, and is thus a definite biologic factor in the evolutional

process. If that is so, it seems probable that the convulsive seizure must have some meaning or purpose in the building up of structure and function. An organism may have to be keyed up to the point of explosion in order to be effective. The existence of epilepsy in groups and colonies may furnish better opportunities for making studies that will throw light upon this interesting phase in the study of the convulsive seizure.

If the epileptic represents a specific type anthropologically and zoologically, there may be found some indication of it in the somatic make-up, just as Dr. Lewis seems to have shown these somatic peculiarities in the paranoid and praecox types of mental disease. There should be a comparative study made of the whole body including all the organs and tissues of epileptics, in order to see if there is any common abnormality. This abnormality may not be in the nervous system, and it may be shown that epilepsy is not a disease of the nervous system but of the whole soma. This is more probable than that there is something peculiar and characteristic in the personality.

# THE ECOLOGY OF EPILEPSY

## II. RACIAL AND GEOGRAPHIC DISTRIBUTION OF EPILEPSY *

C. B. DAVENPORT, PH.D.

COLD SPRING HARBOR, LONG ISLAND, N. Y.

Idiopathic epilepsy may be defined for the purposes of this paper as a tendency, more or less periodic, to convulsions with loss of consciousness, without obvious exogenous factors, and in persons who have an ordinarily well developed brain. Our problem is: what is the distribution in the human species of this tendency to epilepsy?

Three general matters may be discussed at the outset. First, idiopathic epilepsy is not always easy to separate from epilepsy with exogenous factors; for there may be such factors all unknown to the student. Also, even statistics of army recruiting and missionary hospitals do not distinguish epilepsies due to different causes. We shall have to be content with what is available, unsatisfactory as it is. The defect is not so serious, however, since even in cases of epilepsy in which an irritating or inducing "cause" can be distinguished, we can not deny the probable existence of predisposing constitutional factors. Purely exogenous epilepsy is probably relatively uncommon.

Second, epilepsy is one of the most widespread of symptoms. It is found in all races of men; it is found in the animals that we know best—the domestic animals. Examples of these have been cited by L. P. Clark [1] (1904) from the works of Féré and Gélineau. The horse, cat, dog, ox, pig, occasionally the rabbit, and even birds like poultry and the canary may show epileptiform convulsions. Evidently the possibility of clonic contractions of the muscles depends on an architecture of the central nervous system that is common to all of the higher vertebrates; and upon a mechanism which reacts similarly to disturbance of that system. If this is true for mammals as a whole we may expect it to be true for all human races.

Hirsch [2] (1886) indeed says of the whole group of nervous diseases "there is no other so widely spread in time and space and no other has such pronounced, ubiquitous character as epilepsy. The disease is described in all the early medical writings, in the com-

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* Read at the third annual meeting of the Association for Research in Nervous and Mental Diseases, New York, Dec. 27, 1922.

1. Clark, L. Pierce: A Comparative Study of Idiopathic Epilepsy in Animals and Man, New York M. J. **80**:1105 (Dec. 10) 1904.

2. Hirsch, August: Handbuch der historisch- geographischen Pathologie, Ed. 2, Stuttgart, 1886, Vol. III, p. 371.

pendia of the Arabian and of the western doctors of the middle ages; in the medical literature of the sixteenth to eighteenth centuries. . . . The medical-topographical reports of the present time bear witness to the universal incidence of epilepsy over the whole inhabited surface of the earth."

Third, though epilepsy is ubiquitous it does not follow that its proportional incidence is the same in all populations. There are several considerations why we should expect the incidence to vary.

1. Idiopathic epilepsy implies a constitutional basis. Studies by Dr. David F. Weeks [3] and me have, we think, demonstrated the presence of an hereditary factor which acts as a Mendelian recessive. Recessive traits tend to become commoner in a population as it becomes more inbred, provided the defect was present in the ancestry. Thus one of the islands off the coast of Maine, which has been studied by the Eugenics Record Office, reveals an inbred population with a high incidence of epilepsy which can be traced back to the common ancestor of most of the people of the island. Many years ago Dr. Bemiss [4] (1858) reported to the American Medical Association on a collection of 833 consanguineous marriages producing 3942 children, and of these 15 per mille were said to be epileptic. Such facts, which might be multiplied, suggest that we might expect some races in which consanguineous marriages are exceptionally common to show a high incidence of epilepsy.

2. Again, it is sometimes alleged that the drinking of much alcohol induces epileptic attacks and these may recur in the descendants of such imbibers. The epilepsy becomes idiopathic in this strain. If there is anything in this view, countries where little alcohol is used, e. g., India and Turkey, should show a low incidence of epilepsy; countries where strong alcoholic drinks are used to excess, as formerly in Scandinavia, should show a high incidence of epilepsy. At any rate, the existence of the hypothesis justifies the testing of it.

In view of these considerations it becomes desirable to bring together what is known about the rate of incidence of epilepsy in different countries and this is attempted in the following paragraphs from the literature. I take this opportunity to acknowledge the great assistance given by Miss Mabel L. Earle of the Eugenics Record Office in reviewing the literature of this subject.

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3. Davenport, C. B., and Weeks, D. F.: A First Study of Inheritance in Epilepsy, J. Nerv. & Ment. Dis. **38**:641, 1911; Bull. No. 4, Eugenics Record Office, November, 1911.

4. Bemiss, S. M.: Report on Influences of Marriages of Consanguinity upon Offspring, Trans. A. M. A. **11**:321, 1858.

## INCIDENCE OF EPILEPSY IN DIFFERENT COUNTRIES OR RACES

### A. NEGROES

Hirsch [2] (1886) concludes that epilepsy appears in the same form and with equal frequency among the black races of the west coast of Africa as in Europe and other countries. Unfortunately our information as to conditions in Central Africa lacks detail.

Chassaniol [5] (1865) found epilepsy to occur in Senegal much as in Europe, and Bonius (1882) writing from the same place states that epilepsy is of frequent occurrence. Clarke [6] (1860) speaking of the Gold Coast says epilepsy was occasionally brought to his notice.

In the United States we have numerous "negroes," but they are largely mulattoes and, living in contact with the whites, have acquired their vices. Large numbers of such negroes were examined in the army draft of 1917 to 1918 by the same examiners as the white men, and the findings were studied by Love and Davenport,[7] in 1920. It may be instructive to compare the incidence of epilepsy in the two races. In those areas of the Southern States which are inhabited by 45 per cent. or more of "negroes" there was found a lower rate for epilepsy (5.13) than for the prevailingly white Southern agricultural districts (5.65) or for the "mountain white" areas of the south (6.28). This result suggests that "negroes" are somewhat (but only a little) less affected by epilepsy than whites. This accords with a statement of Searcy, who was familiar with the negro race in the Southern States and is quoted by Spratling [8] (1904). He says "it is a generally expressed opinion that insanity and epilepsy are rapidly increasing among negroes." This he ascribes to the removal of the beneficial physical effect of slavery; but it may be equally explained on the ground of increasing hybridization with whites. Modern statistics concerning epilepsy of negroes in the United States are vitiated by the inclusion of mulattoes in the group of negroes.

A careful inspection of Table 1 shows, first, that the rate for epilepsy in the U. S. Army was maximal in the army in the United States in 1918. The rate was high, probably because the army was maintaining in "development battalions" many epileptics who should not have been in the army. The rate was correspondingly low in the

5. Chassaniol: Contributions à la pathologie de la race nègre, Arch. de méd. navale. **3**:509, 1865.

6. Clarke, R.: Remarks on the Topography and Diseases of the Gold Coast, Trans. Epidem. Soc. of London **1**:114, 1860.

7. Love, A. G., and Davenport, C. B.: Defects Found in Drafted Men, War Dept., Washington, Government Printing Office, 1920.

8. Spratling, W. P.: Epilepsy and Its Treatment, Philadelphia, W. B. Saunders Company, 1904.

army in Europe, because these were picked men. In the United States in 1918, the colored rate of 7.23 per mille was a very high one and 2.3 times that of the whites.

During the World War the rate of admission to sick report for epilepsy varied with race as follows:

TABLE 1.—Admission to Sick Report, United States Army, Epilepsy*

| Group | Ratios per 1,000 | |
|---|---|---|
| Calendar Year 1917 | White | Colored |
| Total, United States, Europe, etc | 2.70 | 5.23 |
| United States only | 2.88 | 6.54 |
| United States, only, regulars | 3.04 | 5.49 |
| Europe only | 1.22 | 4.15 |
| Native troops, Porto Ricans | .... | 0.52 |
| White troops in Philippines | 0.64 | .... |
| Philippine scouts | .... | 0.54 |
| Calendar Year 1918 | | |
| Total United States Army, military men | 2.09 | 4.92 |
| United States Army, in United States | 3.12 | 7.23 |
| United States Army, in Europe | 0.81 | 1.49 |
| White troops in Philippines | 1.05 | .... |
| Philippine Islanders | .... | 0.33 |
| Hawaiians | .... | 0.86 |
| Porto Ricans | .... | 5.00 |
| Calendar Year 1919 | | |
| Total, United States Army | 0.88 | 0.92 |
| United States Army in United States | 1.38 | 1.18 |
| United States Army in Europe | 0.67 | 0.92 |
| White troops in Philippines | 1.55 | .... |
| Philippine scouts | .... | 0.12 |

* From Reports of the Surgeon-General, United States Army.

For the year 1917, when we were inducting hundreds of thousands of men into army service, the rate for colored troops in the United States (6.54) was again 2.3 times that for whites (2.88). For the year 1919, when the development battalions had been discharged, the admission of colored troops in the United States (1.18) was less than that of white troops (1.38). Apparently the discharges for disability on account of epilepsy, which in 1918 were (in the United States) 2.4 times as great for colored as for whites, had helped put men of the two "races" on the same plane.

To sum up, the apparent discrepancy between the record of drafted men and that of the army may be harmonized by the hypothesis that in areas with a large proportion of negroes the epilepsy rate was fairly low because the proportion of full blooded negroes was high; so, on the contrary, the "negroes" from other parts of the country, who are really for the most part mulattoes, show a great predominance of epilepsy over the whites. If this hypothesis were confirmed it would support strongly the theory that human hybrids in general are disharmonious, and show a preponderance of nervous defects over the

"purer" races. According to this theory, miscegenation increases the number of new centers of epilepsy; while inbreeding tends to increase the proportion of epilepsies in the descendants of one of them.

Considerable epilepsy was found by Pruner,[9] 1847, in Egypt and from a table of Bertherand [10] (1855) it would appear that among the Mussulmans only (who are forbidden to use alcoholic liquors) epilepsy is an important cause of death.

### B. AMERINDIANS

Dr. A. Hrdlicka [11] made first hand physiologic and medical observations on thousands of pure blooded Indians of our Southwest. Of the Otomi (Hidalgo) Indians, who drink to excess, he says: "epilepsy and other neuropathic conditions are met with frequently." In comparing the Southwestern Indians with average white Americans he says: "Nervous diseases are relatively rare, except epilepsy." Dr. Hrdlicka sent a letter of inquiry to the physicians in the Indian service concerning the incidence of various diseases, including "epilepsy." Reports were received from 102 localities. Epileptics were reported from 47 localities, comprising a population of 70,723 Indians (including half-breeds). There were reported 146 cases, probably all grand mal, in these 47 localities; making a rate of 2.1 per mille. No cases were reported from the other 55 localities. If they had the same population as the 47 reporting epilepsy, the epileptic rate would be reduced to about 1 per mille, which is low. It seems probable that the reporting was far from satisfactory. In certain stations a fairly high rate was reported. Thus among 5,000 Sioux of the Rosebud Agency, twenty-three cases, or 4.6 per mille; among 6,690 Sioux at Pine Ridge Agency, South Dakota, seventeen cases, or 2.5 per mille. It is probable that in migratory tribes the epileptic children die off early. Among 6,600 Pima Indians, at Pima Agency, Arizona, one case is reported, or 0.15 per mille.

In the army draft there were found in South Dakota Indian reservations five cases of epilepsy or 4.3 per mille; in Arizona, Indian Section, (35 per cent. Indians) three cases, or 1.3 per mille; in the New Mexico Indian section (29 per cent. Indians) ten cases, or 8.1 per mille. In the entire "Indian" group, 4.3 per mille epileptics were found, which is less than the average for the whole country (5.2 per mille).

From available data it is probable that the epilepsy rate for Amerindians is slightly less than that for white persons in the United

9. Pruner, F.: Die Krankheiten des Orients, Erlangen, 1847.

10. Bertherand, E. L.: Médecine et hygiène des Arabes, Paris, Baillière, 1855.

11. Hrdlicka, A.: Physiological and Medical Observations Among the Indians, Washington, Smithsonian Inst. Bull. No. 34, 1908.

States. Whether there is a difference in this respect between full blooded and halfbreeds cannot be stated.

Hirsch (1886) states that epilepsy is reported to occur with special frequency in Brazil; but it is not stated that this is true for the Indian population. Also, no ratios are given.

### C. MONGOLIANS

*China.* For this country we have only certain hospital statistics. Thus, in the Medical Reports, Customs Gazette of Shanghai,[12] years 1871 to 1877, are given data furnished by certain medical missionaries. Taking reports where at least one case of epilepsy was recorded during the year (showing that the diagnostic term constituted a class included in the report) we have 21,874 patients and of them sixty-six with epilepsy, or 3 per mille. In Report 58 (p. 74) one case of epilepsy is reported in 400 patients or 2.5 per mille. Dr. W. H. Park reports in 25,000 native patients at Soochow Hospital seventy cases of epilepsy, or 2.7 per mille. In 350 consecutive private cases were two cases of epilepsy, or over 5 per mille. Jeffreys and Maxwell (1910) estimate that epilepsy is probably no less frequent in China than in western lands. Hofmann (1913) finds among 312 insane patients of the J. G. Kerr Hospital at Canton, three or about 10 per mille were cases of epilepsy. Schofield (1882) reports that of 1,851 cases treated at Shansi, North China, eight were cases of epilepsy, or 4.3 per mille. At the Harvard Medical School[13] in China, of 1,438 cases treated medically in 1915 to 1916, five were epilepsy or 3.5 per mille. These are close to the European proportions. Dr. Andrew H. Woods, of Peking Union Medical College, states that among 16,000 patients in the Hospital and outpatient department, he found fourteen cases of epilepsy or not quite 1 per mille. This fourteen does not include organic cases due to syphilis, tumor, embolism and trauma. Dr. Wood thinks that

12. Medical Reports, Customs Gazette, Shanghai, China, Dr. David Mansoris. Reports on the Health of Tahow and Tauwen-foo, No. 3, p. 35; No. 4, p. 24; No. 5, p. 26; No. 8, p. 13; No. 11, p. 25. Dr. A. G. Reid's Reports on Health of Handow: No. 4, p. 72; No. 5, p. 29; No. 8, p. 41. Dr. George Shearer's Report on Cases Treated in Private Practice and in the Kiu Kiang Dispensary for Chinese, 1871, p. 62. Dr. Jardin's Report on the Health of Kiu Kiang, 1875, p. 1. Dr. Scott on Health of Swatow, 1871, No. 11, p. 83. Dr. E. P. McFarlane on the Health of Ichang, 1880, No. 20. Report No. 58, Szemao, 1899; Report No. 59. W. H. Park's Report on the Health of Soochow, 1900, No. 30, p. 5. Dr. H. M. Allen, Health of Seoul, Korea, 1885, p. 17. Schofield, H.: Report of the Medical Mission at T'ai-Yuen-Fu, Shansi, North China, Shanghai, 1882.

13. Reports of the Hospital Department, Harvard Medical School of China, Methodist Publishing House, Annual Report No. 2, 1915-1916; Annual Report No. 3, 1915-1916; Annual Report No. 4, 1916-1917.

the incidence is really much higher, as few cases of petit mal are recorded, and the Chinese would not be likely to bring any but serious cases to the hospital.

*Korea.* Dr. H. N. Allen [12] (1885) reported on the health of Seoul: "Epilepsy is surprisingly common; the worst case yet seen, however, had seizures only twice daily. The disease is considered no bar to matrimony, which may account for its prevalence." In the first 6 months at Allen's Hospital, 7,234 outpatients were treated, 184 for epilepsy or 23.8 per mille.

*Japan.* In the Navy Department of Japan, "Surgical and Medical history of the naval war between Japan and Russia" [14] (1904 to 1905) is a report on 53,657 cases of admission to sick report, eighteen being for epilepsy—this is 0.42 per mille. These were, however, presumably picked men; nevertheless, the rate is low as compared with the 2 per mille admission to sick report in the U. S. Army during the World War. The data establish the presence of epilepsy among the Japanese but do not enable us to judge of its rate in civil life.

### D. EAST INDIANS

Caddy [15] (1901) reports that in 1899, among European troops in India, out of a total average strength of 67,100 men there were eighty-six admissions to sick report for epilepsy, or 1.2 per mille; while among native troops, with a total average strength of 128,530 there were only sixty-three admissions, or 0.5 per mille. Macphail [16] reports that of 7,534 patients treated in his dispensary and hospital in 1904, thirty-six were suffering from epilepsy or 4.8 per mille. In 1834 to 1838, it is stated by the Madras Medical Board Office [17] that of 7,093 admissions of European troops stationed at Malabar and Canara, thirty-two were cases of epilepsy or 4.5 per mille; while of native troops, out of 11,282 admissions only eight were for epilepsy or 0.7 per mille. Of native troops stationed at Calicut: of 1,416 admissions, one was for epilepsy; and of the native troops at Mangalore, of 7,875 admissions six were for epilepsy; together 9,291 admissions, with seven epileptics, or 0.75 per mille. Again of native troops at Hurryhur, 1832 to 1841, of 5,040 admissions, six were for epilepsy, or 1.2 per mille. Of 5,322 admissions of native troops at French Rocks, two were cases of

14. Navy Department, Japan. Bureau of Medical Affairs: The Surgical and Medical History of the Naval War Between Japan and Russia During 1904 to 1909. Tokyo, 1911.

15. Caddy, A.: Trans. Nat. Assn. for the Study of Epilepsy **1**:177, 1901.

16. Macphail, J. M.: Report from India, Trans. Nat. Assn. for the Study of Epilepsy **3**:212, 1904.

17. Report on the Medical Topography and Statistics of the Province of Malabar and Canara, Records of the Medical Board Office, Madras, 1844.

epilepsy or 0.4 per mille. Again, in the Mysore Division: of European troops, among 13,500 admissions, thirty-one cases of epilepsy appeared, or 2.3 per mille; of native troops among 27,085 admissions, eighteen cases of epilepsy or 0.7 per mille.

Bryden's statistics for the Bengal Presidency [18] (1860 to 1863) show: for the European army (strength 43,000), out of 83,406 admissions 147 or 1.7 per mille were for epilepsy; for the native army (strength 37,800), the average admissions were 50,500 of which twenty were for epilepsy, or 0.4 per mille. Even in the jail population the native epileptic rate is barely half that of the European.

From all of these considerations it seems justifiable to conclude that epilepsy is less than half as common in India as in England or the United States; and India uses little alcohol as a beverage.

### E. PHILIPPINE ISLANDS

The admission rate to sick report among native troops of the U. S. Army for epilepsy is about 0.33, or one-third of the rate for white troops in that country:[19] In fact the admission rate for Philippine scouts is extraordinarily low. But this may be due to exceptionally rigid selection.

### F. POLYNESIA

From Mahatly's report [20] we learn that two Fijians and two Solomon Islanders were admitted to, and treated for epilepsy at, the Colonial Hospital, Sura, Fiji. The Senior Medical Officer at Sura states that he has treated cases of epilepsy among Fijians while he was District Medical Officer on the Island of Taviumi and in the province of Ba, but the cases were never numerous and symptoms varied in no way from those among epileptics of other races, particularly Europeans.

Of native Hawaiian troops in the U. S. Army,[19] averaging 2,783, during 1918 and 1919 there was an average admission for epilepsy of 0.54 per mille, which resembles the extraordinarily low rate of the Philippine Islanders.

Thomson [21] (1854) found that in New Zealand no Maoris (who are racially the same as the Hawaiians) had in 1854 been admitted into the hospital on account of epilepsy. He then took some trouble to

18. Bryden, J. L.: Vital Statistics of Bengal Presidency, Calcutta, Government Printing Office, 1871.

19. War Department, U. S. Army, Reports of the Surgeon-General, 1918, 1919 and 1920.

20. Mahatly, A.: Report from Colony of Fiji, Trans. Nat. Assn. for the Study of Epilepsy **4**:290, 1906.

21. Thomson, A. S.: On the Peculiarities of Figure, the Disfigurements and the Customs of the New Zealanders, Brit. & For. Med. Chirurg. Rev. **14**:461, 1854.

ascertain whether the disease had been seen among the Maoris and he concludes: "As I could never meet with a medical man, nor an European who had seen a native with epilepsy, nor a native who could describe the disease, I am inclined to think it does not exist among them, or if it does it must be very rare." Since all the Maoris were derived from a few ancestors (sixteen generations ago) it is quite thinkable that the genetic factors for the epileptic reaction to inciting agents were absent from their constitution.

### G. EUROPE

For the European countries various estimates have been made:

*Switzerland* is of special interest because of the high proportion of consanguineous mariages in the valleys of that mountainous country. Wyrsch [22] (1921) estimates that at Zürich, at least 3 per mille of the population are epileptic. In a rapid survey of the canton Unterwalden with 30,000 inhabitants, fifty-seven cases of epilepsy were found, a rate of 2 per mille; but this is a minimum. Ammann, using mortality statistics, army statistics of 1884 to 1909, and statistics of institutions and schools, concludes that the epileptic rate for Switzerland as a whole is 5 per mille—about the same as for the entire United States.

*Italy,* as a peninsula, has long experienced more than the average amount of inbreeding. According to Binswanger [23] (1899), Morselli found among 5,000 Italians (excluding convulsions in the first two years of life) six epileptics or 1.2 per mille—but this is not significant in absence of further details. Of 10,000 Italian military recruits, 11.53 per mille are said to have been rejected on account of epilepsy—a high rate.

*Germany.* According to Binswanger the rate of admission to sick report in the Prussian Army for the year 1889 to 1890, was 2.1 per mille; for 1895 to 1896, 2.9 per mille. The increase of the rate is ascribed to better means of detection. Among the school children of Mecklenburg, an epileptic rate of 1.15 per mille was found by Tigges,[24] 1883; but this count was incomplete. Estimates of smaller areas have given as much as 2 per mille.

*France.* According to Jolly,[25] French recruit statistics indicate an epileptic rate of 1.6 per mille.

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22. Wyrsch, Jacob.: Zur Frage der geographischen Verbreitung und poliklinischen Behandlung der Epilepsie, Schweiz. med. Wchnschr. **2**:1182, 1921.

23. Binswanger, O.: Die Epilepsie, Wien, Hölder, 1899.

24. Tigges, P.: Die Zahlung der Epileptischen in Mecklenburg-Schwerin im Jahre 1882, Allg. Ztschr. f. Psychiat. **11**:543, 1883.

25. Jolly, F.: Arch. f. Psychiat. **13**:311, 1882.

*Denmark.* No adequate census has been made of the epileptics in this country. An estimate was made of 10,000 giving a rate of 4 per mille; but Soren Hansen [26] concludes that 3,000 is a safer estimate, giving a rate of 1.2 per mille.

### H. GREAT BRITAIN

Fragments of the results of examination of army recruits during 1917 to 1919 have been published.[27] In one section of London the rejections for disabling epilepsy were 0.3 per mille for 1,100 British, and 1.4 per mille for 1,370 Jews (p. 39). In another locality (p. 48), of 2,894 rejections, sixty were for epilepsy, or 20 per mille. In still another locality (p. 113), 37 per mille were rejected for epilepsy. Of 10,000 recruits examined in Scotland, 6.4 per mille were found to have epilepsy of some grade, and 2.5 per mille of a grade requiring rejection.

*Jews.* Fishberg [28] (1911, p. 329) concludes that, despite a predisposition among the Jews to neuroses, epilepsy is less common among them than among non-Jews of the same locality. This is asserted to have been found in Paris, in Vienna, in Frankfort, in Moscow, and at Craig Colony in New York State. Dr. Fishberg states that among 3,000 applicants for relief in the United Hebrew Charities of New York, there is an average of about six epileptics per year, or 2.0 per mille.

### I. UNITED STATES AND EUROPEAN NATIONS REPRESENTED IN IT

The statistics of "Defects Found in Drafted Men" [7] tell something about the distribution of epilepsy in the United States. It appears from the map, p. 92, that the greatest incidence of this disease is in the population of New England, especially Vermont, where the rate was 12 per mille; but also in New Hampshire, rate 7 per mille; Connecticut, 6.9 per mille; Rhode Island, 6.7 per mille; and Maine, 6.5 per mille. Only in Massachusetts was the rate (5.9 per mille) decidedly lower, probably through segregation of many cases in the institutions of this socially highly developed state. Other high rates were found in Maryland, 8 per mille, and Louisiana, 6.9 per mille. These states, except Maryland, contain a large population of French origin. Aside from the maritime districts of the United States (rate 7.10 per mille)

26. Hansen, S.: On Antallet af Epileptikere i Danemark, Ugesk. f. Læger 4:373 and 419, 1897.

27. Galloway, J. H. W. Kaye, et al. 1920. Report upon the Physical Examination of Men of Military Age by National Service Boards from Nov. 1, 1917, to Oct. 31, 1918. Ministry of National Service, 1917 to 1919. London, Stationery Office, Vol. I, 1920.

28. Fishberg, M.: The Jews: a Study of Race and Environment, New York, Charles Scribner's Sons, 1911.

the northern agricultural sections with a predominance of native white stock has the highest ratio (6.7); the mountain white stock of the Southern Alleghanies has also a high rate (6.3). The Southern white agricultural communities have a fairly high rate (5.7) and also the southern section of mainly Scotch origin (5.2). On the other hand, the sections occupied by many Finns, Germans and Scandinavians have a relatively small rate for epilepsy (2.9 to 4.0 per mille).

H. H. Laughlin has recently collected statistics on the relative proportion of the different nationalities who are inmates of American institutions for defectives. These are still in manuscript; he has generously permitted me to abstract certain data. Thus, in nine states, custodial institutions for epileptics found in Massachusetts, Connecticut, New York, New Jersey, Michigan, Ohio, Illinois, Iowa and Texas—all but one in the north—including 6,807 epileptics, the largest proportion in relation to quota (based on population of the race in the United States) was found among peoples from the Turks of Asiatic Turkey, 167 per cent. of quota. Next, immigrants from Great Britain, 145 per cent. of quota; and next in order: Portugal, (133 per cent.), Russia, Poland and Finland, (117 per cent.), Rumania, (114 per cent.) and Ireland, (107 per cent.). Rates below their quota were furnished by immigrants from Greece (45 per cent.), from Austria-Hungary (67 per cent.), Germany (73 per cent.), Canada (75 per cent.) and Italy (83 per cent.). The extraordinarily low rate for Scandinavia (14 per cent. of the quota) is partly due to the fact that none of the states in the Scandinavian part of this country maintain separate state institutions for epileptics. But we have already seen from the Army Draft that the Scandinavian rate for epilepsy is rather low.

TABLE 2.—Summary of Epileptic Rate in Races and Groups

| Class, Nationality or Race, How Obtained | Rate per 1,000 |
|---|---|
| United States: | |
| 2,500,000 drafted men | 5.15 |
| Rural recruits | 5.36 |
| Urban recruits | 4.79 |
| Boston recruits | 6.13 |
| New York City recruits | 5.62 |
| Chicago recruits | 4.53 |
| Vermont recruits | 12.72 |
| Maryland recruits | 7.98 |
| New York Recruits | 6.07 |
| New Jersey recruits | 4.32 |
| Kansas recruits | 3.77 |
| Utah recruits | 3.48 |
| South Dakota recruits | 1.20 |
| Southern agricultural—mainly native white | 5.65 |
| Southern agricultural—mainly negro | 5.13 |
| French Canadian sections | 6.11 |
| Scotch settlements | 5.18 |
| German and Scandinavian settlements | 3.99 |
| Scandinavian settlements | 3.87 |
| Finnish settlements | 2.86 |
| Army, admission sick report, 1918, white (2,204,709) | 2.09 |

TABLE 2.—Summary of Epileptic Rate in Races and Groups.—*Cont.*

| Class, Nationality or Race, How Obtained | Rate per 1,000 |
|---|---|
| United States: | |
| Army, admission sick report, 1918, colored (174,846) | 7.23 |
| Army, admission sick report, 1917, white | 2.70 |
| Army, admission sick report, 1917, colored | 6.54 |
| Scotland, Army recruits, 1917 to 1919 | 6.40 |
| Great Britain | 0.3 to 37.0 |
| British in institutions of United States, 145 per cent. of quota | |
| Denmark, various estimates | 1.2 to 4.0 |
| France, recruit statistics | 1.6 |
| Germany: | |
| Admission to sick report, Prussian army, 1889 to 1890 | 2.1 |
| Admission to sick report, Prussian army, 1895 to 1896 | 2.9 |
| School children of Mecklenburg | 1.15 |
| Other areas | 2.0 |
| Italy: | |
| Morselli's count of 5,000 Italians | 1.2 |
| 10,000 military recruits, rejections for epilepsy | 11.53 |
| Switzerland: | |
| Zurich, estimated | 3.0 |
| Canton Unterwalden, minimum estimates | 2.0 |
| Ammann's estimate for whole country | 5.0 |
| Jews: | |
| Applicants for relief, New York City | 2.0 |
| Russians and Poles in institutions of United States, 117% of quota | |
| Maoris of New Zealand | 0.0 |
| Hawaiian Islanders, admission to sick report, United States Army | 0.54 |
| Philippine Islanders, admission to sick report, United States Army | 0.33 |
| India: | |
| Admission to sick report, Europeans (1889) | 1.2 |
| Admission to sick report, Europeans (1834) | 4.5 |
| Admission to sick report, native Indians (1889) | 0.5 |
| Admission to sick report, native Indians (1834) | 0.7 |
| Missionary dispensary hospital (Macphail), 1904, patients | 4.8 |
| Native troops, Calcutta, admission | 0.75 |
| Native troops, Hurryhur, admission | 1.2 |
| Native trops, French Rocks, admission | 0.4 |
| Troops at Mysore, admission (European) | 2.3 |
| Troops at Masore, admission (native) | 0.7 |
| Bengal Presidency, Army admissions (European) | 1.7 |
| Bengal Presidency, Army admissions (native) | 0.4 |
| Japan, Navy, admission to sick report | 0.4 |
| Korea, Outpatients of missionary hospital | 23.8 |
| China: | |
| Shanghai hospital, patients | 2.5 |
| Soochow hospital | 2.7 |
| Soochow, private cases | 5.0 |
| Shansi, North China, hospital | 4.3 |
| Harvard Medical School in China | 3.5 |
| Amerindians: | |
| Hrdlicka's statistics on 70,000 Indians | 2.1 |
| 5,000 Sioux, Rosebud Agency | 4.6 |
| 6,690 Sioux, Pine Ridge Agency | 2.5 |
| 6,600 Pimas | 0.15 |
| United States Draft, South Dakota Indian reservation | 4.3 |
| Arizona Indian section | 1.3 |
| New Mexico Indian section | 8.1 |
| Negroes: | |
| United States Draft, Negro sections, defect found | 5.13 |
| United States Army, admission to sick report, 1917 | 6.54 |
| United States Army, admission to sick report, 1918 | 7.23 |
| United States Army, admission to sick report, 1919 | 1.18 |

## SUMMARY AND CONCLUSIONS

The tendency for muscles, singly or in groups to undergo tetanic contractions, more or less periodically without obvious exogenous causes, is wide-spread among the higher vertebrates. Consequently, its causative factor must be conceived broadly enough to include mammals and birds. Hence, while alcohol, diet, focal infection and trauma may be, and doubtless are, causative factors in particular cases, yet no one of them is the essential factor. The factor that is most nearly universally present is some constitutional peculiarity of the body that is inherited, so that the tendency for muscles to go "spontaneously" into tetanus recurs with especial frequency in certain families. An, if not *the*, hereditary factor behaves like a recessive. It is a priori probable that certain strains or races differ in the rate of incidence of epilepsy by virtue of either an inherited constitution, or a difference in the incidence of one or more exogenous factor, or by virtue of both of these causes.

Probable low incidence of epilepsy was found among the primitive Maoris, perhaps because the constitutional factor had not been brought in by the few immigrant ancestors. Some Amerindians appear to have a low rate by virtue of the early elimination of those showing symptoms. Otherwise, the rate is possibly slightly below that of the United States generally. Probable low rates are found among the East Indians, possibly due to low incidence of alcoholism; also among full-blooded negroes of the Southern United States. Soldiers of Philippine and Hawaiian Island stock have low rates. Apparently the same is true for Japanese naval men. In the United States territory populated largely by Finns, Germans and Scandinavians, the rate is low. Prohibition Kansas, and states occupied by the antialcoholic Mormons, have exceptionally low rates for epilepsy. In general, both favorable endogenous and exogenous factors are probably responsible for low rates.

High rates are found, apparently, in Korea, which as a long inhabited peninsula has probably an inbred population in which the incidence of the endogenous factor has become intensified. Italy, also a peninsula, seems to have a high rate among military recruits. The rate is high in some parts of Great Britain, an island. If these rates are reliable they indicate the danger of inbreeding in a population with the endogenous factors. In the United States high rates of incidence are found in sections where there are many French Canadians. Also Maryland has a high rate; whether or not this is causally connected with the strong pro-alcohol sentiment in the state, can naturally not be determined.

In general, the statistics suggest that alcohol may be an important exogenous factor which influences the epileptic rate; but doubtless the endogenous or constitutional factors are no less important.

# EPILEPSY AND THE CONVULSIVE STATE*

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"As the departments of science become more and more complex, definition is recognized as a scholastical task which makes for sterility." An epigram by Sir Clifford Allbutt, which like all such obiter dicta can only be half true. To define explicitly may be futile or impossible; to describe, to classify and to set boundary marks can be done with difficulty, maybe, but always with advantage to clarity of ideas.

The effort to define may fail in ultimate truth, but will show us often the scope of our endeavor and the nature of our objective.

The idea of epilepsy which came to us from Hughlings Jackson is that it consists in the occasional sudden excessive violent discharge of some nerve center, sensory or motor; to which it would seem useful to add that the phenomena produced are independent of volition and are accompanied by interference with the stream of consciousness. Events of this general character—and not all epileptic phenomena can be covered even by this ample cloak—happen under such varied conditions, and in such a motley company of diseases that the notion is forced on us that the convulsive state and transient paroxysmal changes in consciousness cannot represent any single disease entity in themselves. They are but the expression of an innate or induced instability of nervous centers from diverse causes, operating, it may be, through a common constant connecting mechanism. Therefore, it may happen that the direction of search should be toward the nature of that mechanism which allows nervous explosion to occur—a quest which must range from cardiovascular ataxia to chronic intoxication and the protean appearances of anaphylactic shock.

It is vital to recognize, on the one hand, the essential unity of all attacks of loss or impairment of consciousness often accompanied by convulsions, and, on the other, the heterogeneous nature of conditions which may give rise to such attacks.

We cannot too vigorously insist on the frequently fleeting character of such epileptogenous conditions, nor combat overzealously the portentous, and miserably untrue prognosis saddled on such disorders by the public and many of our profession.

We are so familiar with epilepsy produced through renal disease and the poisonings of an uneasy pregnancy, that by granting such epilepsy special titles, we have obscured the fact that epileptic events in

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certain individuals follow hard on the heels of intoxications and are curable by the removal of the toxic material. Ignoring these facts, we arbitrarily classify cognate, often identical, phenomena in a category of disaster, whereby the diagnosis of epilepsy has become synonymous with a sentence to perdition. Epilepsy has been described by some of the most eminent writers on the subject as a condition characterized by recurrent convulsions and terminating in dementia. Surely this statement reveals but a fragment of one end of the spectrum of this disorder. True, the context usually attempts to adjust the ill balanced values set out by this description, but the context is apt to be difficult and the definition easy of quotation, the result being the unwisely restricted viewpoint so often taken of the condition and the often foolishly lugubrious outlook imposed on the subject and his friends. These remarks have been directed at those who would damn the future of the patient suffering from occasional convulsions or their isolated auras, but of late a group of writers has sought to blacken by quite improper emphasis, the moral and mental antecedents of the unhappy persons liable to this dyscrasia.

Thus it has been asserted that the individual destined later to recurring convulsions is shackled by a character ethically depraved; that he displays an egocentric contraction of the entire emotional life; that he is a pathologic liar, a distrustful pertinacious fellow given over to weak rages and black vapors. I imagine that such a portrait has been painted in a badly lighted studio rather than from life.

Every physician, of however slight experience, sees Calibans and Timons who never had a fit, and men of high moral and intellectual quality subject to the disorders we now discuss. However, premises of this character, or lack of character, are necessary to permit the psychologic interpretation of epilepsy submitted by this screedy school. A personality so misshapen and so warped must in self-defense commit occasionally psychologic suicide, must be allowed to dip itself in Lethe, to banish the horrid awareness of itself; in short, to have a fit in which it seeks the Nirvana of the womb, to search again periodically for its pristine purity and innocence by the resuscitation of impulsive fetal movements! Job cursed the day he left his mother's body, but it has been left to the minor poets of a less humorous age to make him investigate the possibility of resuming an umbilical attachment! My translation of this theory is perhaps too simple—but here is its original kernel (I have no means of knowing whether or not it has felt the displeasure of an irate compositor): "We are justified in considering the essential nucleus of the epileptic fit an infantile unconscious striving of displeasure-pleasure pursuit ending in the final goal of a return to infancy, attended by a loss of consciousness and a convulsion; that the convulsion is made up of and flows out of the general striving of the

fetal and infantile tissues as expressed through the lower spinal centres in inducing simple and crude combinations of impulsive movements; that a study of the degree of development of unconscious infantile strivings in the emotional instincts, the desire for an infantile state of omniscience (sic) are paralleled by the kind and character of impulsive movements found in this infantile period of neuromuscular development."

"The epileptic reaction from its mildest to its severest manifestation is really a protection, for it obliterates reality and reduces the subject to the lowest level of organic response, that of the comatose state. It dispels an intolerable demand and the epileptic retreats to a state of harmony and peace."

One wonders why a nocturnal epileptic in a fit of self-hatred should have to retreat from the harmony of slumber to that of coma. However, we are finally informed that these lucubrations "give us a more rational understanding of the nature and mechanism of the disorder itself and render the plan of handling and treating the essential disorder more understandable and practicable." Now, of course, they do nothing of the kind. On the contrary, jargon of this sort fails to throw even so much light as shone in Milton's Hell, for that at least made visible the darkness and caused the traveller to walk delicately therein.

It is a simpler task, however, to say what epilepsy is not, than what it is. It has been already described as an occasional paroxysmal discharge of a nerve center or group of centers occurring apart from volition and accompanied by interference with consciousness. Perhaps "impairment" might be a better word than "discharge," for many of the minor manifestations have such negative characteristics as to preclude the use of so positive a descriptive title. Even in the major seizure, the sequence of events can be most readily understood as a sudden cutting out of the highest level, the cortex, allowing the lower neuronic levels to pour downward an ungoverned stream of tonic postural impulses—in fact, an abrupt rigidity of the decerebrate type. The subsequent convulsions which have secured, by their dramatic quality and their greater duration, more attention than I think they deserve, probably represent the gradual return of cortical control, incapable, at first, of ordered volitional action. I suggested at the beginning of this paper that many diverse causative conditions must operate through a common mechanism to produce so constant a result, difference in the various manifestations of epilepsy, from the major for my claim is nothing less than a qualitative unity and quantitative seizure through petit mal, to migraine, to recurrent syncope and periodic endogenous emotional tempests. And in the gamut I should include, without equivocation, the voluminous mental states of unreality, and those prolonged and terrifying experiences known now as vasovagal attacks in which the patient is suddenly terror-stricken, suffers medi-

astinal oppression, has a feeling of tingling and swelling of the limbs, a sense of impending death and, losing precision of contact with his surroundings, experiences an acute transient seizure of cardiac hurry. Hughlings Jackson believed "idiopathic epilepsy to be far too difficult a subject for precise investigation unless we approach its consideration from the bases supplied by the principles deduced from the less complex kinds of cases." Probably the mechanism of the major attacks will be revealed by a study of the manifestations of the minor attacks which will be found, I think, to be fragments of the fully developed seizure—just as we have fragments of the decerebrate posture produced by imperfect mesencephalic block, so we may have fragments of the great fit produced when abnormal conditions, probably of a vascular nature, are not sufficiently violent to unseat the entire cortical function.

The vasovagal attack which I have just described, if condensed in point of time, would be the same as the phenomena of many of the petit mal attacks, and I can personally vouch for its identity with the sensations felt when, having compressed my carotids and vagi, I lost control of my experiment and, a few seconds later, of consciousness.

Leonard Hill, more intelligently and successfully—but, of course, less heroically!—compressed one carotid in himself: "the first effect was a sensation in the eye of the same side; then there followed a sensory march of formication down the opposite side of the body. This began in the fingers, spread up the arm and down the leg. Finally, clonic spasms of the hand occurred, accompanied by an intense feeling of vertigo and alarm." Whether clonic movements occurred in my own case, I do not know, as I was alone at the time and have since lacked inclination to repeat the experiment; the sensation in the hands and forearms for the few seconds before loss of consciousness, was that of very powerful faradization; it was still present on my recovery but quickly passed away.

In connection with these considerations of vascular change, it is proper to remind ourselves of the cerebral phenomena produced by severe heartblock. Thomas Lewis finds that suspension of the mental functions is produced by a single period of asystole of from three to seven seconds' duration. In severer cases, where the pulse ceases for fifteen seconds or more, there occur cyanosis and stertor, and twitching of the face and limbs; fatal status epilepticus is by no means infrequent. In such cases there is a cessation of general circulation, but in the cats operated on by Stewart and Pike, cerebral and medullary circulation only were cut off. The immediate results were unconsciousness and bladder and rectal evacuation, severe tonic convulsions, then flaccidity (it must be remembered that midbrain circulation was obliterated); after the return of circulation there were clonic convulsions which prefaced resumption of consciousness and complete recovery.

In the ability of the emotions to cause severe vasomotor fluctuations and, in certain persons, syncope, and in certain others, headache or minor and major convulsions, we have an approach to a psychologic mechanism in epilepsy, which differs as has already been suggested, from that impressionistically sketched by Pierce Clark and others.

One cannot leave the subject of vasomotor instability in epilepsy without mentioning the remarkable case published by Osler of Raynaud's disease of the fingers, feet, ears, and nose, occurring during six winters and accompanied only during such seasons by severe epileptic convulsion.

Such events raise again the question of the existence of motor nerves in the cerebral blood-vessels. These were thought for long to be absent, but Gaskill's observations have demonstrated their presence; the muscular walls in these vessels would seem evidence enough, but Biedl and Cushing have both made manifest that epinephrin blanches the brain as it does other tissues, and Wiggers has shown a definite diminution in the outflowing blood after the addition of epinephrin to the fluid circulating through the brain.

John Hartwell and I were once able to observe the brain of a patient during a general epileptic fit; the exposure of the parietal cortex had been carried out under local anesthesia whereby consciousness and normal reflex activity were retained up to the moment of the attack. The initial sign of the seizure was a sudden whitening of the cortex which was no sooner remarked on than it was replaced by tremendous venous engorgement with protrusion of the brain beyond the level of the bone defect. This alarming engorgement, in which the previously blanched cortex became beet color and many of its veins swelled to half the diameter of one's small finger, was coincident with the tonic stage of the attack and the period of general clonic convulsion. The cortex failed to recover its normal appearance during the remaining twenty minutes of exposure, though its blood-red color was gradually mitigated in that period. The engorgement was apparently a part of the diffused cyanosis consequent on the general tonic spasm; the initial chalky appearance, however, must have been due to a vascular constriction which, I believe, was the proper beginning of the cerebral seizure.

Cushing has shown that faradic stimulation of the cortex produces pallor of the gray matter and it might be well to bear his observation in mind when considering what exactly we mean by the spread of focal attack. Such spread is too slow to be explicable by the passage of a nerve impulse and might well be dependent on a quickly widening area of cerebral anemia. McRobert and Feinier advanced recently an interesting theory to account for the fact that generalized epileptic seizures result more often from neoplasms in the temporosphenoidal

lobes than from tumor formation in any other cerebral area. These observers believe that the topographical relation of the sylvian artery to these lobes renders the former susceptible to abrupt compression from the transient edemas surrounding the growth; such sudden devascularization, they believe, renders the cortical elements unstable, but as I have already suggested, the mechanism may be rather that the cortex is cut out by such an event and lower levels released by lack of adequate control.

Following up the notion that the initial tonic phase of the grand attack is due to a stream of ungoverned impulses from the lower neuronic levels, we might remember that, in spinal convulsion due to strychnin poisoning, there is no initial tonic period and that clonic spasms occur from the beginning, whereas from midbrain intoxication by either tetanus or rabies, there occurs engravescent tonicity—lockjaw and risus sardonicus—or tonic convulsion as the first manifestation of disease. It would appear that the discharges of energy produced by strychnin poisoning would be included in the definition of epilepsy advanced by Hughlings Jackson, as would indeed those associated with rigor, simple shivering or that curious somatic tremor which some people experience after micturition. It is for this reason that I have thought it necessary for clinical purposes to make it clear that we consider as medically epileptic only phenomena associated with interference with consciousness. It is not desirable to say that, in what Gowers called the borderland of epilepsy, there is impairment of consciousness, for in the voluminous mental state there is often a feeling of expanded receptivity, a subjective enlargement of the orbit of awareness, a sense of prescience. We must not deny the possible expansion of consciousness in such events merely on the grounds of their subjectivity—our sense avenues are the usual, but—in the light of the new physics—may not be the sole pathway of ethereal impulses! However, an extraordinary acuteness of reaction to sensory stimulation may occasionally be seen in epileptic persons. Convulsions could be produced without fail in two patients under my observation. In one, a child, by flicking or sharply tapping the left side of the nose, in the other, an adult, by rubbing the dorsum of the left foot. The attack in the first case consisted in immediate dilatation of the pupils, tonic spasm of the arms and chest, respiratory arrest, cyanosis and slight frothing at the mouth, the whole lasting sometimes fifteen, sometimes twenty seconds, and ending in flaccid exhaustion after return to consciousness. There were no clonic movements in this child whom Dr. Jackson was good enough to come to the hospital to see and whose fit he regarded as a typical bulbopontine explosion.

In my second case, who was under the care of Dr. Farquhar Buzzard, the convulsions were general and followed the usual pro-

cedure of a major seizure. The right parietal cortex was exposed in this case without anything of note being revealed.

In 1920 there was admitted to the neurological department of Bellevue Hospital, a boy aged 17 years whose history stated that for twelve months he had been subject to instant falling to the ground on hearing a sudden sound—a horse pawing the ground in a quiet street, a boy whistling behind him—would be enough to produce cramp in the left leg and a quick fall in which he was always bruised. He denied any loss of consciousness and certainly to onlookers, gave for a long period, no evidence of such. However, after two years of these events, frequently repeated, he had a major convulsion which came on after the slamming of a door and was preceded, as were the other attacks, by a feeling of cramp in the leg. These larger seizures did not entirely replace the fallings after sudden sounds. I induced both types of attack with ease, but did so rather seldom as he would fall violently on his face and, so innocent was he of any reflex of defence, I feared for his safety.

This is an example of the reflex acusticomotor epilepsy described by Oppenheim; for many months, the boy was thought by some competent men to be hysterical. His first fall occurred at school when he was trying to solve a tough problem at the blackboard; his crayon broke and he fell sharply to the ground—a refuge, perhaps, from his embarrassment—indeed an admirable example of a sly subliminal mitigation of Fate! His infantile history, however, supplied an organic background if not an organic explanation. Three weeks after birth there was still present a very large caput succedaneum over the right occipitoparietal area. This was opened and a blood clot evacuated. There was said to have been a bone defect in this area at that time. Symptoms of meningitis are said to have been present during the first two weeks of life. When five months old he had a general convulsion; later, he began to have jerky movements when falling asleep and on waking; in his mother's words: "The left leg would come up and the left shoulder and body go forward; the movement would occur eight or ten times but varied in number and intensity." These hypnogogic events lasted with lessening severity for fourteen years; two or three years later they were replaced by the recurrent episodes just described.

The parietal cortex was exposed. A great thickening of the dura was discovered, produced by an old organized, subdural clot. The attacks have become rare since the operation, and hypersensitiveness to sounds uncommon. This boy always stood near the top of his class; he is now in his second university year, an athlete of splendid physical development, and his peculiarly sweet character scarcely coincides with the sonorous descriptions of ethical and emotional depravity described

by some as being both the cause and the result of maladies such as his. This case has been told at some length because of its intrinsic oddness, but also because, while refuting emotional torment as the cause of organic cerebral explosions, it shows how a brain can be sensitized by trauma and react quickly to stimulation either by primary discharge or in answer to rapid vasomotor changes.

It is needless to discuss here the exact relationship between migraine and epilepsy; they are both found in persons of neuropathic type and heritage: both diseases often occur in different persons of the same stock and very many instances are reported where they existed at different times in the same patient. In a case of my own, the left-sided headache was ushered in by a sensation of flashing lights in the right temporal field, numbness in the right hand, and ingravescent hemianopia, alexia, and aphasia, all of which became practically complete. The subsequent headache lasted for some hours during which the patient behaved rationally. Following the seizure he had complete amnesia for the period of the attack with the exception of its first half-hour.

Migraine has been reported as alternating in three patients with family periodic paralysis—but it would be futile to list here the numberless forms of equivalents which have been described and are entirely familiar to this audience. Earlier in this paper I used the term the spectrum of epilepsy. My general purpose has been to suggest that in this spectrum are many colors which merge insensibly into each other; uremia and eclampsia of pregnancy, the fits of general paralysis and brain tumor are there: the spasmophilic conditions of infancy are also to be thus grouped, including certain forms of tetany associated with confusion of consciousness: the chorea of pregnancy may be in this spectrum also, and—not very deep in the ultraviolet sector—are probably some cases of major hysteria, the motor phenomena of which suggest the temporary abandonment of a cortical for an infracortical mechanism.

Turner divided all these symptoms into: the organic epilepsies arising from trauma, and focal organic disease of the brain; the early epilepsies, those of childhood and infancy, often accompanied by infantile cerebral hemiplegia or mental retardation; the late epilepsies, emerging from chronic disease of the heart and blood vessels, or from intoxications by alcohol, lead or syphilis, and those springing from eclamptic conditions; lastly he sets down "idiopathic, essential, or genuine epilepsy, a malady arising about the period of puberty, usually progressive, difficult or impossible of arrest and fathered by no tangible or ascertainable cause." I submit that while all these maladies most properly are called epileptic, their arbitrary subdivision gives an air of unlikeness to their descriptions, incompatible with fact and that there is no ground for defining "genuine epilepsy" as an isolated group except that in the

other groups, causative factors have already been discovered. Analysis has been almost overdone; synthesis of these symptoms displays their essential unity. Idiopathic tetanus has only recently been obliterated by the discovery of the cause of the disease; and to this was added shortly, its prevention, mitigation and cure. It is that the same may happen to idiopathic epilepsy that we labor today.

# SYMPTOMATIC EPILEPSY IN BIRDS

## AN ANATOMICO-PATHOLOGIC AND CLINICAL REPORT

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From the literature of comparative zoopathology it seems that epileptiform convulsions due to lesions of the brain are rather frequent in birds. Yet the pathologic findings have not always been studied. For this reason, I am reporting the case of a chicken which for several months had shown convulsive attacks, of jacksonian type, in the right wing.

### REPORT OF CASE

*Clinical History.*—The chicken of medium size, in April, 1918, began to show a constant tendency to fall toward the right. Sometimes it would fall and lie on this side; it would then rise again, walk fifteen or twenty steps and fall again. Later it began to be attacked with clonic spasms of the right wing and foot, with a tendency to rotate the head toward the right, and frothing at the mouth. The attack would last from fifteen to twenty minutes and leave the animal somewhat confused. During August, about four months after the onset, the convulsive attacks became more frequent, and occasionally occurred several times a day. They were always of the same type. Towards the end, the chicken became unable to walk; it would try to elevate the right leg, but at every effort would fall, always to the right. To advance, it would lean against the wall for support on the right side. The chicken always lay on this side, and invariably rotated the eyes downward at intervals. Finally, as the convulsive attacks became more frequent, the bird was killed on September 17, 1918, five months after the onset of the symptoms.

*Necropsy and Microscopic Examination.*—On the ventral surface of the right half of the pons (Fig. 1) was an irregular depression two millimeters in diameter which, to palpation, gave an impression as if there were very hard tissue beneath the surface.

The cerebrospinal axis was hardened first in formaldehyd and later in Müller's fluid; it was then embedded in celloidin and cut in frontal serial sections from the proximal extremity of the prefrontal lobe to the conus medullaris. The sections were stained by the Weigert-Pal or the Pal-fuchsin method. No lesions were found anterior to the point of exit of the seventh pair of cranial nerves.

In a transverse section at the exit of the seventh pair of nerves, the area corresponding to the right tractus tectobulbaris cruciatus in its ventromedial portion, was partly decolorized. The specimen also revealed the disappearance of some fibers of the trapezoid body, mainly on the right side; the most dorsal fibers of this body remained intact. In a frontal section of the pons in a plane distal to the preceding one, the area of the tractus tectobulbaris was degenerated, especially on the right side.

The transverse sections of the pons (Fig. 2) at the level of the abducens nucleus, contain a focus which appears as a small mass of black pigment (melanin) of circular shape, and occupies the right ventromedial region of the pons. The fibers of the tractus tectobulbospinalis cruciatus are greatly

rarefied on the right, and much less so on the left. The ventral radicular fibers of the sixth nerve are also involved in the disease focus on the right side.

A frontal section at the proximal end of the medulla oblongata (Fig. 3) reveals an area, corresponding to the ventromedial portion of the right side of the pons, which is replaced by a substance, chocolate brown in color externally, and yellowish internally, which contains fat globules, fragments of myelin fibers, and hematoidin crystals (broken down blood clot). The borders of this focus are irregular and serrated, and the surrounding tissue has lost its nerve fibers. The focus has destroyed all fibers of the right tractus tectobulbaris cruciatus up to the neighboring fibers of the tractus tectospinalis, and extends, beyond the raphe, into the extreme ventral portion of the homologous region of the left side.

Before discussing the clinical features of my case, it may be well to mention the little that has been published on the subject. Marek [1] simply states that birds are subject to epileptic attacks. Friedberger and Frohner [2] say that epilepsy is not rare in birds, especially parrots, canaries and chickens. Friedberger particularly describes a convulsive

Fig. 1.—Ventral aspect of the brain of the epileptic chicken. The right half of the pons is depressed and transformed into a dark tissue of cicatricial appearance.

attack in a chaffinch. During the attack this animal shook, lost consciousness and had violent clonic spasms of the muscles of the extremities; it fell on its back and remained in one place with legs and wings extended, and with the head drawn backwards; the beak and eyelids were successively opened and closed, and the eyeballs were rotated. Finally, consciousness was rapidly restored. Marek says that birds in convulsive attacks, first emit loud cries, shake, and fall on one side, or on the back; the feet then jerk rapidly, the eyes are strongly rotated, the head is drawn to one side, and the beak opens and closes. Exceptionally, there is shaking of the whole body. The convulsions disappear after one or two minutes, and the animal remains stupefied for some

1. Marek: Hirnblutung bei einen Kanarienvogel. Allatorvosi lapok, Budapest **31,** 1908; cited in Ellenberger Sch. Jahrsb. d. vet. Med. 1908, p. 363.

2. Friedberger und Frohner: Lehrbuch der spez. Path. und Ther. der Haustiere, Stuttgart, Enke, 1904, p. 737.

time. It then rises, wanders about for a while, and supports itself with its beak and extended wings.

Reimann and Beyer [3] describe a cock which was frequently attacked with convulsions of the legs. It would fall and rise, and then finally rise again and eat with appetite. The necropsy disclosed dilatation of the heart and atrophy of the walls of its ventricles. (The brain was not described). Bruno [4] mentions a canary which showed unilateral paralysis, and died from cerebral hemorrhage. This was confirmed by necropsy. Sustmann [5] mentions epileptiform attacks in a gray parrot. Reimann [6] reports a cock affected with inflammation of the joints of

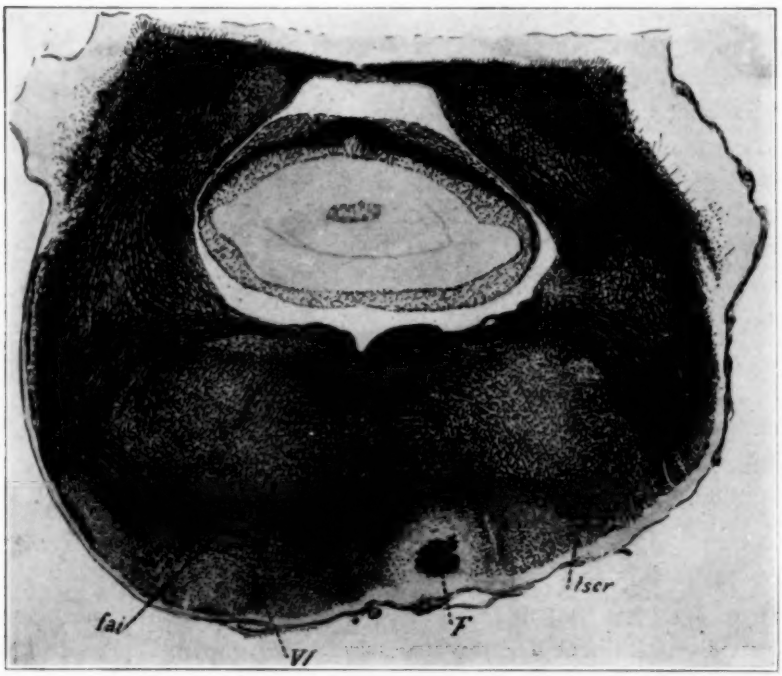


Fig. 2.—Transverse microscopic section of the pons at the proximal pole of the hemorrhagic focus. F, hemorrhagic focus; tbe, tractus bulbospinalis cruciatus; tb, bulbar portion; tscr, spinal portion; VI. abducens nucleus; fai, internal arcuate fibers.

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3. Reimann und Beyer: Krankheits und Sektionsbefunde, Dresdner Bl. f. Geflugelzucht, 1888; cited in Ellenberger Sch. Jahrsb. d. vet. Med., 1889, p. 187.

4. Bruno: Ueber Hirnblutungen bei Kanarienvogeln, Gior. d. r. Soc. d. Accad. vet., 1902, p. 513; cited in Ellenberger Sch. Jahrsb. d. vet. Med.

5. Sustmann: Epileptiforme Anfälle bei einen Graupapagai, Münch. tierarztl. Wchnschr. **66**:121, 1915.

6. Reimann: Krankheits und Sectionsgeschichte, Dresdner Bl. f. Geflugelzucht, 1886; cited in Ellenberger Sch. Jahrsb. d. vet. Med., 1887, p. 139.

a leg caused by mechanical injuries, which developed, almost suddenly, in addition to the local disturbances, a peculiar nervous syndrome. The animal drew the injured leg up to the abdomen, and kept it well stretched out behind him and extended upward; the bird then again retracted the leg on the abdomen, and followed this by touching the foot to the floor with quick jumping jerks, and finally started to use it properly. No necropsy was performed. The same author states that, in cerebral hemorrhage in birds, retropulsion and disordered movement have been observed. The necropsy made by him on a cock that had been walking backwards and turning to the left around itself with head rotated, revealed hemorrhages into the cerebellum and pons, besides acute hyperemia and edema of the right half of the brain.

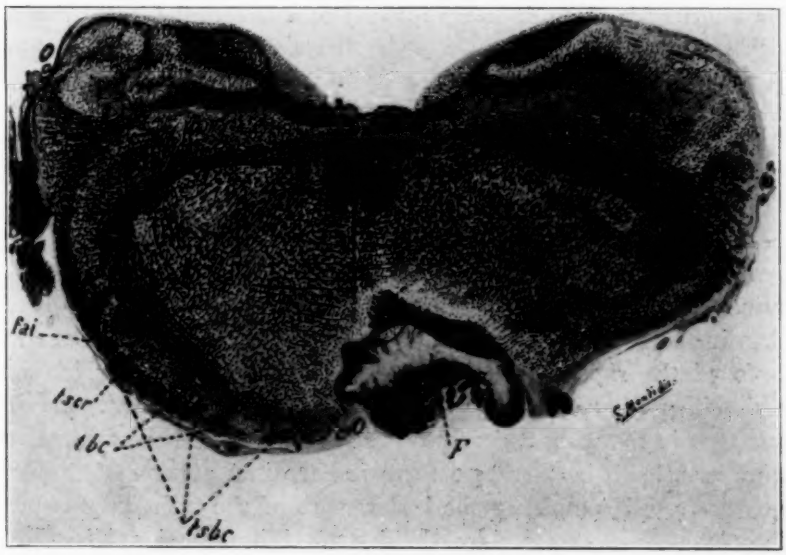


Fig. 3.—Transverse microscopic section of the pons at the level of the abducens nucleus where the hemorrhagic focus had reached its greatest extent. The focus destroys all the fibers of the tractus tectobulbaris cruciatus and part of those of the tractus tectospinalis. F, hemorrhagic focus; tbc, tractus bulbospinalis cruciatus (tb, bulbar portion; tscr, spinal portion); fai, internal arcuate fibers.

Marek mentions the case of a canary which, in its fits, rotated the head obliquely toward the left, and moved around in a circle toward the right, with the left wing down. There was found at the necropsy an extravasation of blood in the left pes pedunculi which corresponded to a frontal section made between the corpora quadrigemina and the nucleus of the sixth nerve.

In the chicken which I examined, convulsive attacks, distinctly unilateral, of the wing and leg occurred during several months, and

were followed by progressive paresis of the same parts. The necropsy disclosed a hemorrhage in the ventromedial portion of the pons.

Birds may, therefore, have the syndrome of essential epilepsy; general convulsions of classical epileptic type, which involve the eyes, beak, head, wings, and legs. Observations of lesions of the brain in such cases are as yet lacking. In addition, birds may have attacks of symptomatic epilepsy, which result from lesions of the cerebral hemispheres or of the basal portion of the pons. My case here cited, is an example of the facility with which epileptiform attacks are developed in chickens in consequence of a hemorrhage into the pons.

In man, spasms due to lesions of the pons, have been observed shortly after the inception of a rapid lesion (abscess, hemorrhage), and after a certain time in slowly progressive lesions, such as tumor. Such attacks are more or less transitory and affect muscles of one side which are already paretic; or else they consist of twitching and spasm of the face, and rotation of the eyes in different directions (Monakow). Unilateral convulsions which generally affect the opposite half of the body have often been observed; more frequently there occur general convulsions. It has not yet been determined what particular structure of the pons, upon irritation, gives rise to these attacks. Nothnagel believed it possible that general motor irritative manifestations might arise from the pons alone; whereas Bechterew held that spasms in pontine lesions depend on indirect irritation of the cerebral hemispheres in the Rolandic area. In my chicken the symptoms began with paresis of the right wing, foot and abducens nerve, to which were added, either simultaneously or soon after, convulsive attacks of a clonic type in the wing and foot on the same side. Microscopic examination revealed a hemorrhagic focus in the distal portion of the pons, which destroyed completely the bulbar part of the right tractus tectobulbospinalis cruciatus and partly destroyed its spinal portion. The lesion extended to the left beyond the raphe.

As is well known, voluntary motion, so-called, is subserved in birds by the tractus tectobulbaris and tractus tectospinalis; the latter, according to Edinger[7] occupies the lateral portion of the lateral periphery of the mesencephalon; hence, in all probability, it is located in the corresponding position in the pons. Now, as the fibers of the tractus tectobulbaris were in my case almost all destroyed, and those of the tectospinalis were badly damaged, we can understand why there were at times symptoms of permanent deficiency and at other times evidences of irritative phenomena. Human pathology offers numerous similar examples, especially following destructive focal lesions in the

7. Edinger: Vorlesungen über den Bau der nervösen Centralorgane des Menschen und der Thiere, Leipzig, F. C. W. Vogel, 1911, Vol. 2, Fig. 88.

rolandic region or in the pes pedunculi. Comparative anatomy has also taught us that the complex of bundles of the above named tracts decussates mostly in the mesencephalon and then passes along the ventral margin of the pons. It is therefore easy to understand why symptoms of irritation and of deficiency, caused by partial lesions of these tracts on the right side of the pons, were present in the extremities of the same side. The tendency to the formation of a cyst and the development of cicatricial tissue, explains why the paretic-irritative syndrome had become more marked during the last months. This case, which meets the requirements of an experiment, demonstrated that, at least in birds, the tractus septomesencephalicus cannot be considered identical with the tractus corticospinalis from the functional point of view, as some believe; but instead, that the tractus tectospinalis is to be considered as equivalent to the tractus corticospinalis of the higher mammalia, since irritation of the latter will give rise to convulsive attacks of a clonic nature, with at the same time paresis of one side. Therefore we may conclude that these physiologic properties of the tectobulbar and tectospinal tracts have been transported by phylogenetic evolution into the neophyletic motor tracts (tractus corticospinalis). They come, not from the tectum as do the paleophyletic ones, but from the cortex cerebri, and have developed beneath the first, which, in birds, pass along the ventral border of the trunk of the encephalon.

# INFANTILE PROGRESSIVE MUSCULAR ATROPHY OF WERDNIG-HOFFMANN TYPE

## CASE REPORT WITH NECROPSY *

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Twenty-one years ago Werdnig [1] published the first description of the clinical and necropsy findings of the syndrome which has since borne his name. Two years later Hoffmann [2] described the pathology of one case, gave the clinical notes of three others, and confirmed Werdnig's conclusions. The literature at present contains studies of about fourteen typical, non-congenital cases, only six with histopathologic findings. The first cases recorded in the American literature were those of Bliss in 1916.

In 1900, Oppenheim [3] described a syndrome, now known as amyotonia congenita, which he observed was not hereditary nor familial but rather congenital; a tendency toward improvement was characteristic, and the seat of the principal pathology was thought by him to be in the muscles. Subsequent to Oppenheim, Spiller,[4] Lereboullet and Baudouin,[5] and Councilman and Dunn [6] reported necropsy observations confirming those of Oppenheim. Spiller and Lereboullet and Baudouin, however, found only slight changes in the muscles, and the spinal cord to be practically normal. Thus anatomic studies in amyotonia congenita revealed lesions similar to those found by Werdnig and Hoffmann.

Holmes [7] reports a case of amyotonia congenita and emphasizes the similarity between the pathologic findings in the familial, progressive, non-congenital form (Werdnig-Hoffmann) and those of amyotonia congenita. Krabbe [8] reports six cases of congenital and familial

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* Read at the annual meeting of the Central Neuro-Psychiatric Association, Rochester, Minn., Oct. 21, 1922.

1. Werdnig: Arch. f. Psychiat. **22**:706, 1891.
2. Hoffmann: Deutsch. Ztschr. f. Nervenh. **3**:427, 1893.
3. Oppenheim: Monatschr. f. Psychiat. u. Neurol. **8**:232, 1900.
4. Spiller: Univ. Penn. M. Bull. **17**:342, 1904.
5. Lereboullet and Baudouin: Bull. et mém. Soc. méd. d. hôp. de Paris **36**:1162, 1909.
6. Councilman and Dunn: Am. J. Dis. Child. **2**:354 (March) 1911.
7. Holmes: Am. J. Dis. Child. **20**:405 (Nov.) 1920.
8. Krabbe: Brain **43**:166 (July) 1920.

spinal muscular atrophy and one of the hereditary, non-congenital, progressive type, all with similar clinical and pathologic findings. He concludes that there are two types of amyotonia congenita: one is the non-hereditary, favorable variety with muscular hypotonia but no definite atrophy; the other shows atrophy of the anterior horn cells and muscles, and usually has a positive hereditary and familial history. Huenekens and Bell [9] report a case of the Werdnig-Hoffmann type with a positive hereditary history, as well as the familial history that a previous child probably suffered from amyotonia congenita. They give a list of typical and atypical cases. It would seem that their atypical cases could properly be classed under the second group of the grave congenital types of Krabbe. Reuben [10] has summarized the pathologic findings in cases of amyotonia congenita which had been reported up to April 1917. Barton [11] has reported a familial noncongenital case with necropsy. Duken and Weingartner [12] submit a complete case report with familial and congenital history. The three cases of Knox and Powers,[13] in which necropsies were not performed, belong in the congenital category. The report of Leenhardt and Sentis [14] leaves one in doubt about their first case; their second case apparently is not congenital. In neither case was there a necropsy.

Thus it appears that the main clinical distinctions between amyotonia congenita and the disease of Werdnig-Hoffmann are: (1) the hereditary, familial or congenital origin; (2) the presence or absence of atrophy; (3) the course of the disease, as regards its tendency toward progression or recovery. The relation of the necropsy findings to the clinical picture is not definite, and it is obvious that a clear understanding will not be reached until more cases with histopathologic findings are reported.

## REPORT OF A CASE

*History.*—Annie M. was admitted on March 14, 1921, to the out-patient service of Dr. Bronson Crothers at the Children's Hospital. She was born at full term on Jan. 15, 1921, and was the sixth child of healthy, Italian parents. Delivery was easy and natural, and the child was breast-fed. Muscular activity during the first month of life was normal. The child gained in weight and was apparently well until the age of one month. During the second month, weakness in arms and legs had been progressive.

*Family History.*—The first child in the family is well and aged 6 years and 9 months. The second, third, fourth and fifth children died at the ages of 3, 4, 5, and 4 months, respectively, all from pneumonia. All had a period of

9. Huenekens and Bell: Am. J. Dis. Child. **20**:496 (Dec.) 1920.
10. Reuben: Arch. Int. Med. **20** (Nov.) 1917.
11. Barton: Lancet **2**:922 (Nov. 22) 1919.
12. Duken and Weingartner: Ztschr. f. Kinderh. **29**:245 (July) 1921.
13. Knox and Powers: South. M. J. **13**:86 (Feb.) 1920.
14. Leenhardt and Sentis: Arch. de méd. d. enf. **24**:137 (March) 1921.

"paralysis" before death, similar to that of the case here reported. In other words, the familial factor in this case is conspicuous. No further details of the history were obtainable.

*Examination.*—A normally developed, plump baby, aged 2 months, who was apparently comfortable. She gave a weak cry at times. The head was of normal shape, and the anterior fontanel was open, though there was no bulging. The cranial nerves were normal. The arms and legs were moved very little, though the limbs on the right moved more than those on the left. The toes flexed on stimulation but there was no motion at the hips or the knees. The arms moved at the elbows, wrists, and fingers. The knee and ankle jerks were absent. There was no Babinski sign. No definite atrophy, group paralysis, spasticity, or contractures were present. The abdominal muscles and the external muscles of respiration were all weak. Breathing was diaphragmatic in type. The electrical reactions were normal with a fairly strong faradic current and with a galvanic current of 5 milliamperes. Sensation was normal and the results of further physical examination were negative. No Wassermann test was made. The spinal fluid was not examined. A roentgenogram revealed a heavy fat layer, and apparent atrophy of the muscles of the arms and legs.

*Course.*—March 23: The right arm flexed easily at the elbow, the left did not flex so easily. The fingers of both hands flexed and extended fairly well. The legs were flaccid, and motionless except for the occurrence of plantar flexion of the toes. It was very obvious that muscle tone had diminished since March 14. A reaction of degeneration was now present. No reaction was obtained in the rectus abdominis muscles.

April 4: Weakness of the forearm muscles was quite marked on both sides. Movement of the toes was weaker.

April 18: Reaction of degeneration and weakness was further advanced. A pulmonic infection occurred during the last days of April and the first part of May.

June 6: Reaction of degeneration was complete in arm, leg, and trunk muscles. A roentgenogram of the trunk revealed normal viscera and spine. After this visit to the out-patient department, the patient again developed a pneumonic affection and death occurred June 23, 1921, seven days after the last hospital examination.

Fibrillary twitchings were not noted at any time. The diaphragm was not involved, and the facial muscles did not give the reaction of degeneration. As the child was not an in-patient of the hospital, the study of the case was not satisfactory.

*Necropsy.*—A necropsy, performed by Dr. Cobb twelve hours after death, was restricted to an incision over the spine. The length of the body was 95 cm. The abdomen was protuberant; the thorax was funnel shaped and small, with very thin muscles. The pectoral muscles were particularly small and soft. The buttocks were normal. The pupils were round and equal, and measured 3 mm. in diameter. The hair was thin, and there were brown, scaling macules on the scalp. The anterior fontanel measured 3.5 by 3 cm. and was depressed. There was no discharge from the ears or from the nose. The genitals were normal. There was an unusual configuration of the anus; a band below caused the anus to point almost straight backward. The subcutaneous fat layer over the back was about 7 mm. in thickness. The muscles were pale and soft, and of fibrous appearance and consistency. Specimens were taken which included: (1) A thin sheet of the latissimus dorsi. (2) The

right brachial plexus. (3) The right hamstring muscle. (4) The left sciatic nerve. (5) The spinal cord and most of the medulla. The only gross abnormality of the cord or membranes, was a slightly purplish discoloration of the dura mater over the lumbar enlargement. Spinal fluid was taken by cistern puncture. The thymus, adrenals, viscera, brain and other muscles and nerves could not be examined.

Examination of the spinal fluid gave negative results with Wassermann and globulin tests.

*Histopathology.*—Sections of the medulla, below the lower portion of the vestibular nucleus, reveal no changes in the nuclei of the ninth, tenth, and

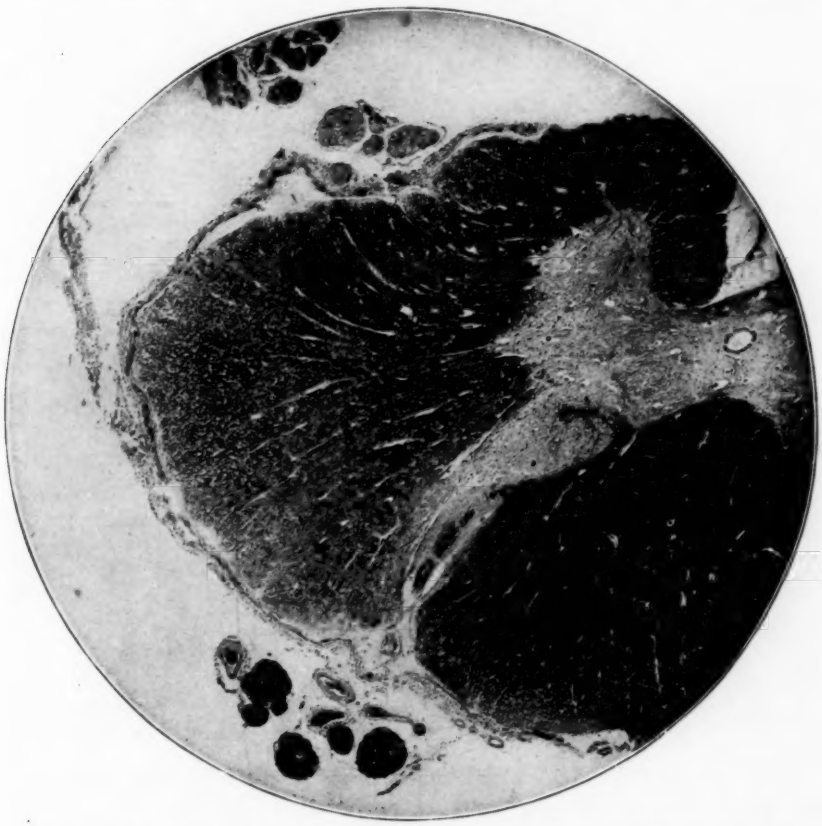

Fig. 1.—Thoracic segment of spinal cord showing normal myelin in dorsal roots but partial degeneration of ventral roots. Van Heuman stain.

twelfth cranial nerves. Root fibers of these nerves are normal. There are no connective tissue nor glial abnormalities. In the cervical region of the cord (cresyl violet stain) the total number of cells is reduced. In one section there are three normal anterior horn cells on one side and five on the other. The cells which remain are reduced in size. They show signs of chronic degeneration; the chromophil substance is closely packed, and the cells appear small and dark. Cells in the dorsal horn are normal. The Marchi stain reveals no acute degeneration of the myelin. Phosphotungstic acid stains show no altera-

tions in the neuroglia. The ventral nerve roots, within the white matter of the cord, as well as outside of the cord substance, show, by Weigert's method, marked diminution of myelin. The contrast between these and the normally stained dorsal roots, is quite pronounced. Other structures are not involved.

One section from the thoracic region of the cord contains but two normal nerve cells in one ventral horn and four in the other. The remaining cells are attenuated and show chronic changes similar to those in the cervical sections, with the exception that one cell has swollen, pale cytoplasm, and an eccentric

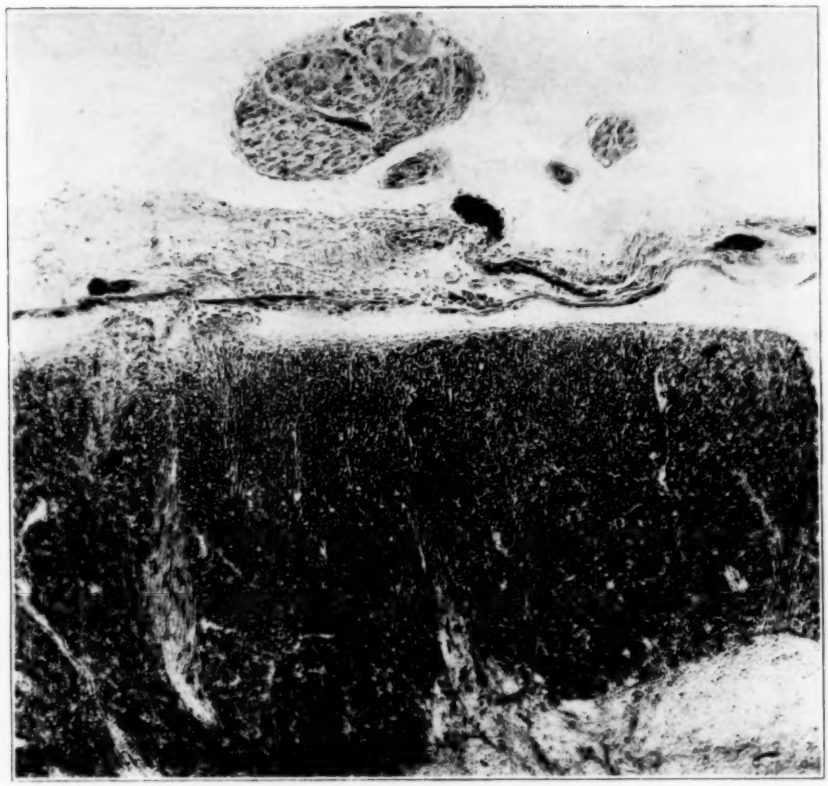

Fig. 2.—Ventral root of lumbar segment of spinal cord showing degeneration, as evidenced by lack of myelin. Van Heuman stain.

nucleus, a condition of acute degeneration. The cells in Clarke's column and the dorsal horns are normal. Van Heuman's[15] stain shows marked diminution of myelin in the ventral nerve roots (Fig. 1). The Marchi method demonstrates phagocytes in the blood vessels, laden with darkly staining bodies which are evidently fat particles. No other changes are shown by this method. Phosphotungstic acid slides are negative. In the lumbar region of the cord there is marked diminution in the number of ventral horn cells; about one third of those which remain in one ventral horn are normal, and in the other ventral horn one

15. Van Heuman, Luden: Centralbl. f. allg. Pathol. **23**:98, 1912.

fifth are unchanged. The chronic cell changes described above are prominent. Acute changes are demonstrable in smaller numbers. All other parts of the section, except the ventral nerve roots, are normal. Weigert and Van Heuman stains reveal striking diminution of myelin in the ventral roots (Fig. 2). The phosphotungstic acid and Marchi stains give negative results. Cross sections of parts of the brachial plexus stained by Van Heuman's method, show many nerve bundles devoid of myelin. Other bundles have only little normal myelin. The blood vessels and supporting tissues are not altered. The myelin changes are

Fig. 3.—Latissimus dorsi muscle showing small muscle fibers, with increase of connective tissue about some individual fibers, and a relative increase of connective tissue throughout the whole area. Mallory's connective tissue stain.

also present in a terminal nerve within the hamstring muscle. Cross section of the left sciatic nerve shows changes like those of the brachial plexus. Cells of the neurilemma sheaths are not changed.

Sections of the latissimus dorsi (Fig. 3), hamstring and erector spinae muscles show marked atrophy of many fibers, but the small fibers appear to be fetal in type rather than degenerated. Normal fibers may appear in atrophied fasciculi, or whole bundles of fibers may be normal. Frequently a whole bundle is atrophied. Some of the smaller fibers have the appearance of smooth muscle; cross striations are lacking. The picture is not that of secondary atrophy.

There is marked, relative increase of connective tissue, but only slight true fibrosis. This is evidenced by an occasional muscle fiber, surrounded by a fine network of connective tissue. No fatty changes are noted.

### COMMENT

The similarity of these pathologic findings to those noted in the "second form of amyotonia congenita" of Krabbe, and in the familial type of Werdnig-Hoffmann, would indicate that these two syndromes should be regarded as a single disease entity. Whether symptoms appear before birth, as suggested by the absence of intra-uterine movements, or whether they do not present themselves even before the second half-year of life, would seem an insufficient criterion for the separation of the two syndromes, since the myelopathic processes do not seem to be distinguishable. The amyotonia congenita of Oppenheim, however, (with its pathologic changes limited to the muscles, and with a favorable prognosis) as originally described, should be regarded as a separate and more restricted syndrome.

# CYSTIC BLASTOMYCOSIS OF THE CEREBRAL GRAY MATTER

## CAUSED BY TORULA HISTOLYTICA STODDARD AND CUTLER *

WALTER FREEMAN, M.D., AND FRED. D. WEIDMAN, M.D.

PHILADELPHIA

The diffuse form of blastomycosis of the central nervous system appears as plastic meningitis which may be combined with cystic infiltration of the gray matter. The central nervous system is involved chiefly, and sometimes apparently primarily, and the causative organisms are found in the meninges and in the cysts.

### REPORT OF A CASE

*History.*—H. P., a man, aged 39, was under the care of Drs. Charles H. Frazier and William G. Spiller, at the University Hospital from May to July, 1921. On admission he complained of severe paroxysmal headache of one months' duration. The headaches were progressive and were not localized. Projectile vomiting had occurred daily during the week preceding admission. The eyesight had become poor during the preceding two weeks. He was aware of no loss of memory, aphasia, weakness or difficulty in walking, and had had no convulsions. A short time previously he had had temporary difficulty in writing his name and in talking clearly.

Six months before admission a small mass had appeared on the right eyelid. This was diagnosed by a dermatologist as epithelioma, and disappeared under radium application. In 1911, his tonsils were removed and later some cervical lymph nodes became enlarged. In 1916 one of these was excised and after microscopic examination was pronounced to be Hodgkin's disease. The cervical nodes diminished in size under radiation but at the time of admission the patient had a large discrete mass in the right axilla.

*Examination.*—The patient was talkative, and somewhat facetious. On examination there were disclosed: moderate rigidity of the neck, nystagmus in looking to the left, slight exaggeration of the tendon reflexes and a positive Kernig sign. The optic papillas were elevated five diopters. There were no localizing signs, and in view of the negative findings in other organs a tentative diagnosis of unlocalized brain tumor was made.

The spinal fluid escaped under a pressure of 55 mm. of mercury; it was clear and formed a pellicle on standing. The cell count was 315. Thirty per cent. of the cells were typical lymphocytes, 6 per cent. were leukocytes. The remaining cells were round or oval with greenish, highly refractile bodies and a few intracellular granules which did not resemble nuclei. Many presented a double contour, and some were obviously budding. Smear preparations were not satisfactory.

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*Course.*—During the two months after admission to the hospital the patient became gradually worse. The headache became constant; left ophthalmoplegia developed; and, a few days before death, there were several generalized convulsions which were followed by weakness, loss of tendon reflexes and stupor. The temperature ranged between 99 and 100 most of the time, and did not rise above 101. The blood count, blood culture, urinalysis and Wassermann tests were all negative. The blood serum did not agglutinate the organism that was found, and was too anticomplementary to be used for complement fixation tests. Lumbar punctures relieved the headaches.

*Necropsy Record.*—A necropsy was performed eight hours after death by Dr. Balduin Lucké. External examination was essentially negative. The lungs showed hypostatic congestion but there was no pleuritis or consolidation. The heart was slightly enlarged and flaccid. The alimentary tract and pancreas were normal; the liver presented signs of an early atrophic fibrosis, and the kidneys showed marked tubular nephrosis with degeneration. Enlarged lymph nodes were found in the right axilla and in the mesentery, the largest of which measured 9 by 5 by 2.5 cm. The spleen was also enlarged. Both grossly and microscopically the glands presented an unusual picture which was characterized by loss of architecture, enlargement of the follicles, and infiltration with large, deeply staining cells which contained one or more nuclei.

The coincident enlargement of the spleen and lymph nodes, with a history of ten years' duration, suggested Hodgkin's disease, but the characteristics of the nodes, both grossly and microscopically, differed from the description given by Reed. The larger cells were too deeply stained, fibrosis was practically absent, and there were but few eosinophils. No yeast organisms were found in the sections but by means of guinea-pig inoculation they were recovered from the gland at the head of the pancreas.

The calvarium and cerebral dura showed no abnormalities. The fluid in the basal cistern and ventricles was cloudy, and contained numerous blastomyces. The brain was large and soft. The pia was not injected but was moderately thickened and edematous. A few minute pearly gray nodules were found over the convexity and in the great longitudinal fissure. *No cysts were seen until after formaldehyd fixation.* No areas of softening or tumor formation were detected by the palpating finger. After formaldehyd fixation the pia appeared thick and opaque. It stripped very readily, and then exposed a cerebral cortex in which cysts were so numerous at some places as to resemble soapsuds. These minute vesicles were raised slightly above the surrounding surface, and were sharply differentiated by the transparency of the contents. On section, the contained material did not flow but was of mucoid consistency. The external walls of some cysts were extremely thin but none appeared to have ruptured. Section through the brain revealed an extraordinary number of small cysts, some were almost a centimeter in diameter, whereas, others approached the limit of visibility. They were usually multilocular but always rounded. They were limited to the gray matter of the cortex and basal ganglions. The soapsuds appearance was also present in the cerebellum. The brain stem and spinal cord appeared normal. The spinal pia-arachnoid was slightly more thickened than the cerebral.

No focus of infection was found in the middle ear, accessory sinuses, or nasal or pharyngeal cavities.

*Microscopic Examination.*—The pia-arachnoid was considerably thickened by edema and fibrous tissue hyperplasia, together with cellular infiltration. Some

of the cells were lymphocytes and plasma cells, but most were large cells with faintly granular cytoplasm, and a large vesicular nucleus which was sometimes multiple. These cells formed collars about the pial vessels and extended out into the meshes of the tissue; some contained blastomyces. A few yeast cells lay free in the meshes of the tissue. No encysted or mycelial forms, and very few budding forms, were seen. No polymorphonuclear cells were present.

The outstanding abnormality of the cortex was the presence of the cysts, the great multitude of which gave rise to the soapsuds appearance mentioned in the gross description. They were scattered very irregularly; sometimes large ones were present at the surface and small ones beneath, sometimes the reverse arrangement existed. Large superficial cysts sometimes overlay one or two of smaller size. All, except the very minute ones, appeared to be multilocular and the partitions consisted of cerebral tissue (Figs. 1 and 2). Some cysts were well filled with organisms, phagocytic cells, and detritus; in others the fluid portion greatly exceded the formed portion, and the cells were present only at the boundaries. The cysts appeared to form by internal expansion, which was due to the growth and multiplication of the organisms and the exudation of fluid, rather than to liquefaction necrosis. The cavities were sharply defined in almost all instances, though no special lining was present. Extension took place by direct progression, and by infiltration along perivascular sheaths. Many of these sheaths were dilated and contained phagocytic giant cells and yeast cells. There were no cysts in the subcortical white matter, though some of the perivascular sheaths were dilated and contained a few yeast cells and phagocytes (Fig. 3).

Giant cells were derived from the vascular adventitia. The cells became larger and more rounded, their nuclei dividing by fission. The larger cells took up organisms. Within the cells, these blastomyces developed capsules and distended the cells to very large dimensions—from 50 to 70 microns in diameter. The cytoplasm was disrupted, the nuclei were displaced, and the outline became irregular and indefinite. Finally the cell walls appeared to rupture and the organisms were set free in the cavity.

The nervous tissue immediately surrounding the cysts was compressed to some extent, the ganglion cells were elongated and flattened, their processes were distorted, and in the septa they were displaced toward one another. Generalized distortion of the cyto-architecture was not seen, except close to the cysts. Chromatolysis was general, and a few cells were undergoing neuronophagia and other forms of destruction; but, except in the immediate vicinity of the cysts the cells appeared relatively normal. Fine nerve fibers were found in the trabeculae and cyst walls. Stains for fat showed that a small number of cells about and within the cysts, and along the perivascular spaces, contained fatty material. There was no notable increase in neuroglia, nor infiltration of the chronic inflammatory type. There was very little blood pigment. The yeast cells were concentrated in the cysts and perivascular spaces, and were not found in the intervals. The walls of the vessels appeared normal; no organisms were found in their lumens.

In the basal ganglions, the cysts were mostly of small size and were situated at a distance from the ventricle. A similar cystic condition was present in the cortex of the cerebellum. Here the cysts were smaller, but more numerous, especially in the superior vermis.

The brain-stem contained many minute cysts in the gray matter around the aqueduct of Sylvius and in the floor of the fourth ventricle. A focus was found in the left oculomotor nucleus that accounted for the ophthalmoplegia which

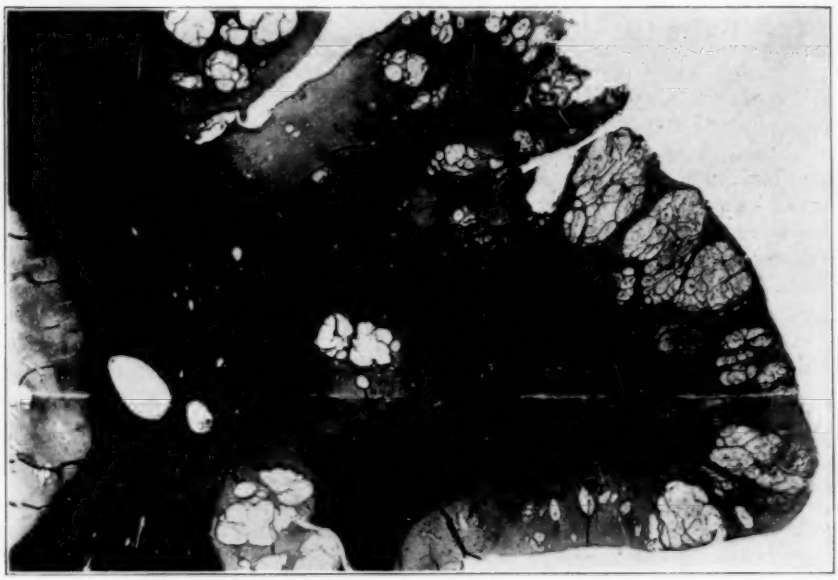

Fig. 1.—Multilocular cysts, limited to the cortex, in the frontal lobe. The pia has been stripped.

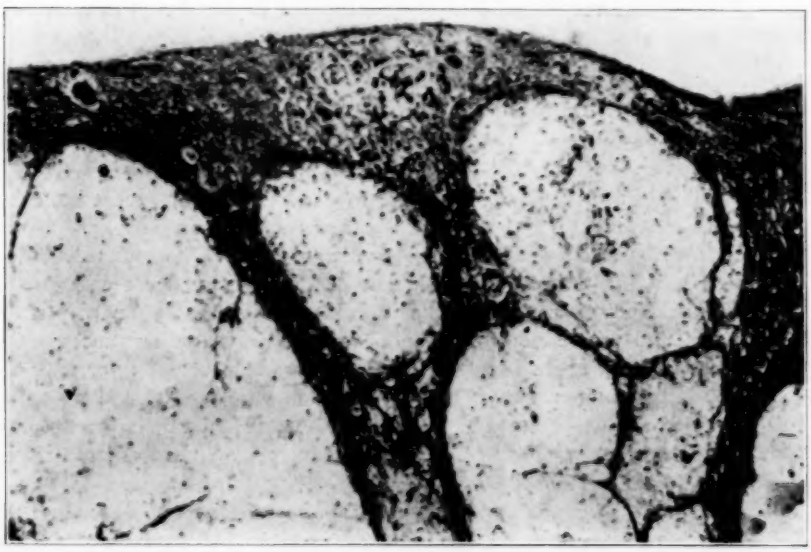

Fig. 2.—Part of a multilocular cyst, close to the surface. The most superficial cyst is recent. The others have enlarged as the result of exudation and expansion of the mucoid envelopes of the blastomyces.

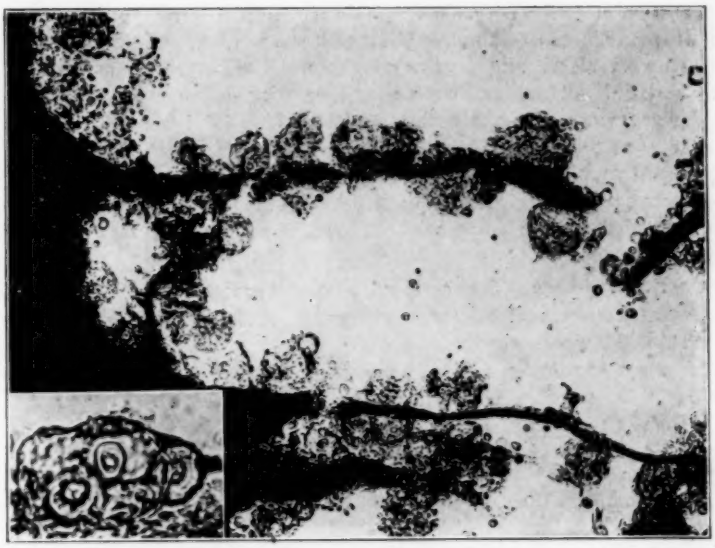

Fig. 3.—Phagocytic giant cells in cavities. A few organisms are free in the cavity. The insert shows a more highly magnified giant cell. Frozen section. Toluidin blue.

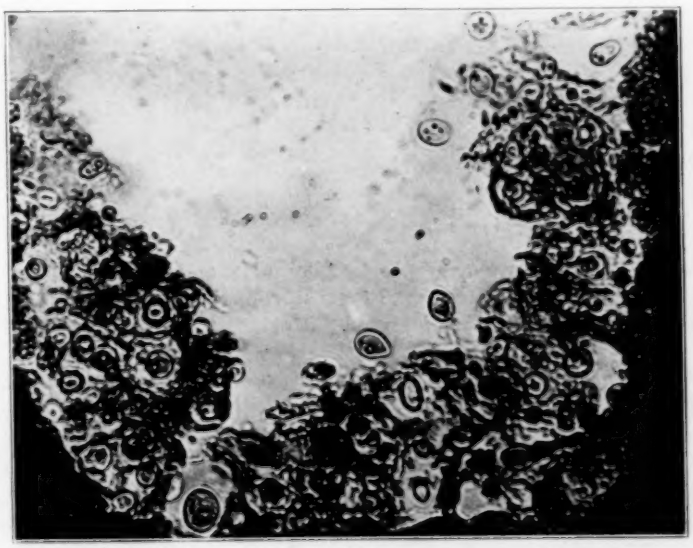

Fig. 4.—Torulae in a cyst. The morphology of the organisms is well shown. The halos are vague. On the right is a multinucleated phagocytic cell. Frozen section. Toluidin blue.

had been observed during life. There was a focus also in the pyramidal tract where the myelin sheaths were disrupted and a cystic condition was developing. The optic nerve contained numerous small cysts of spindle shape, which lay between the fasciculi and separated them. The myelin sheaths were not invaded and did not appear swollen or otherwise degenerated. The meninges over the base were moderately infiltrated with fluid, yeast cells, and phagocytes. Many of the vessels had large collars of these cells (Fig. 6).

The spinal meninges were more compact than the cerebral, and here and there blastomyces were found. Giant cells were scarce. The cord substance was not invaded by the organisms. There was no degeneration in the projection tracts.

*Histologic Summary.*—The cerebral cortex, basal ganglions and cerebellum showed great numbers of minute cysts which varied markedly in size. They contained blastomyces, phagocytes, fluid and detritus. Destruction in both gray and white matter seemed to have resulted from the pressure due to the growth of the cysts. The reaction on the part of the host's tissues was almost

Fig. 5.—Torula with a capsule. Frozen section. Basic fuchsin.

negligible. There was no neuroglia proliferation, and little or no inflammatory cell exudate. The discovery of yeast cells in the dilated perivascular sheaths suggests that extension followed this route.

### THE FUNGUS

*Technic.*—In tissue which has been embedded, many yeast cells, especially the young forms, suffer so much distortion that they may be unrecognizable as yeasts. Even with the mature forms, it is better to avoid embedding processes and to use frozen sections to bring out the finer structural details, and to examine the tissue either when unstained or after staining with watery solutions of toluidin blue, thionin or basic fuchsin. The yeast cells should be examined in a watery or alcoholic medium. Clearing the sections with glycerin or xylol is to be avoided. To bring out the mucinous envelope, we stained over night at 50 C. with dilute aqueous solution of basic fuchsin. In such tissue preparations, budding and younger forms of the yeast were scarce, and the coarsely granular forms with double contour were numerous. The extracellular yeast

cells tended to be small, to contain small numbers of granules, to be sometimes apiculate or ellipsoidal, and frequently to have double contours. Their form thus corresponded to that of old cultures (adverse environment). Intracellular forms were larger, had larger and fewer granules, thick shells, and sometimes a very heavy hyaloid (mucinous) coating. This mucinous envelope did not give the tinctorial reactions of mucin and was eventually demonstrated in material from cultures as well as in the tissues.

*Cultural Characters.*—Primary cultures were obtained from spinal puncture fluid only on blood agar. Trials on plain mediums were unsuccessful but subcultures thereafter grew well. These primary cultures, and the earlier ones on potato, lacked the strong yellow color of later subcultures. On blood agar

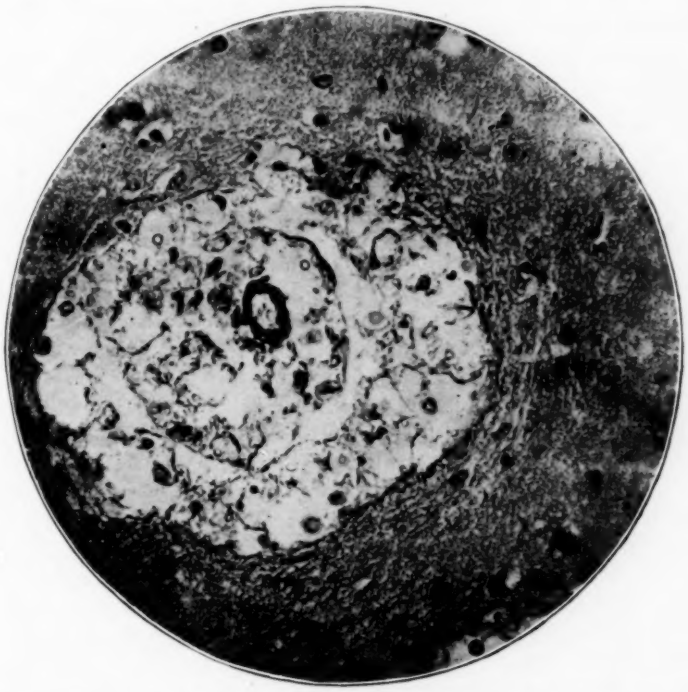

Fig. 6.—Extension of yeast cells along a perivascular space. Yeast cells, phagocytes and detritus are shown. Hematoxylin-eosin.

they were white, and on potato yellow-gray. On the latter the growth was very abundant. Further observations were made over a period of several months.

The organism grew well at body temperature, and equally well at room temperature in semi-darkness, on glucose agar, plain peptone agar, beer-wort, and glucose agar to which gentian violet, in the proportion of 1: 100,000 had been added. Plantings on solid mediums included both plate and tube plantings. As usual with yeasts, growth was most luxuriant on the several carbohydrate mediums. The growth on glucose agar will be described as the type, and the variations on the other mediums will be noted later.

In tube cultures, the outstanding naked eye characters of the colonies were their rapidity and luxuriance of growth, the strong yellow color, the uniformly

round contour and the highly glistening surface. As compared with control cultures—*Saccharomyces cerevisiae*—this yeast grew fully as rapidly at first, and ultimately excelled and developed even to twice the bulk of the control. The margin of the colony was sharp, moderately elevated, rounded, and regular. The yellow color developed only after four weeks in the earlier cultures, but in later subcultures it developed much more promptly, in from seven to ten days. The organism did not penetrate downward into the medium nor discolor it in the least. When the tube cultures were from six to eight weeks old, or when mediums for any reason began to dry out, the colony reflected the desiccating process; its color became yellowish-brown, and its surface less glistening. But it never developed any special surface markings such as furrows, wrinkles, foldings, peripheral radiations, or wedges. On no kind of medium, solid or liquid, was there ever any naked-eye evidence that mycelia were being produced.

On gentian-violet glucose agar, the characters of the colony itself were unchanged. The organism was very resistant to the dye, and it was necessary to add gentian-violet to the medium in the proportion of 1:1,000 before growth was restrained. This property may be useful in securing pure primary cultures from tissues.

On plain peptone agar (containing no carbohydrates) a non-characteristic white colony, three to four millimeters in diameter, developed. By the naked eye it could not be distinguished, at any age, from many other yeasts. It had the same general, more or less dirty-white, homogeneous, pasty character.

In beer-wort, Guilliermond's formula,[1] the growth became evident by a faint cloudiness of the medium, and a delicate ring of scum which was attached to the walls of the tube at the surface of the medium. By the end of two weeks, the scum had become a thin pellicle; there was a granular growth adherent to the sides of the tube from the top to the bottom, and a moderately heavy sediment. The medium was clear until agitation dislodged the surface particles.

When grown in Petri dishes, the changes in color and consistency proceeded much more rapidly than on the thicker strata of medium in tubes; and the colonies, even when the medium was prevented from drying out, never grew as large. The streaks had the common pasty, homogeneous character of yeasts. They showed a yellow color as early as the fourth day and in four weeks they became brownish-yellow. The streaks never become more than a centimeter wide; the edges never were fuzzy enough to indicate mycelial development; and none of the lumpy characters, such as Türk has described for his yeast, were ever developed.

In glucose-agar stabs at the end of twenty-six days, the surface of the culture was completely covered by a colony of burnt-orange color. In the depths of the stab there was a well developed growth, almost as heavy at a depth of five centimeters as at the surface. Fine granules could be seen projecting from the margin of the stab. There was no evidence of gas production.

In fermentation tests it was found that late subcultures of the organism split sugars slowly. No gas was produced in glucose, maltose, saccharose, lactose, galactose, inulin or dextrin mediums at any time. Acid was produced in only four of these seven sugars (saccharose, glucose, maltose and dextrin), and then but slowly.

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1. Guilliermond, A.: The Yeasts, English translation by Tanner, New York, John Wiley & Sons, 1920, p. 150.

*Morphology.*—Our yeast was identical morphologically with that of Türk and, since he has so well portrayed it, we shall but briefly describe it. The appearance of individual yeast cells varied markedly in accordance with their age. Mature forms were spherical with double contour, pale green in color, and of about the same size as *Saccharomyces cerevisiae.* The earliest budding examples were coarsely granular, but in a few days cultures were found also to contain large cells with a double contour and a solid, hyaloid, spheroid body, which almost or quite filled the interior. In cultures several weeks old the central part of such a cell contained, instead of the single body, from two to eight or more larger or smaller hyaloid spheroids. These were variable both in number and size. We, therefore, finally concluded that they were not asci. Buds could be found springing from any of the above forms of cell after three weeks, in all the mediums used, solid or liquid.

Inasmuch as the subject of asci is so important for classification, we tried all of the cultural and staining methods which have been recommended by

Fig. 7.—Cells from two months' old culture showing mucoid capsules. India ink method.

Guilliermond for bringing out these structures, and controlled our results with *Saccharomyces cerevisiae.* Asci failed to appear and we finally concluded that this organism does not produce them.

Mycelial structures were found in only four of the culture tubes from a dozen examined, and then in the condensation-water at the bottom of the glucose agar tubes which were two months old. Hence, it must be concluded that the filamentous form of this organism is most exceptional. It is not to be considered in classification.

Attempts, by staining methods, to demonstrate a mucinous envelope on organisms from culture were unsuccessful. We finally detected it by making an emulsion of yeast cells with India ink and examining them at once under a coverslip (Fig. 7). A brilliant, refractile halo appeared around many of the older cells, but only from cultures several months old. The substance of this envelope must be a product of old cells only, and probably of cells that are experiencing an unfavorable environment.

CLASSIFICATION OF FUNGUS

In the present stage of yeast classification, there is but little incentive to attempt to place pathogenic yeasts into exact taxonomic positions. Guilliermond [1] following Vuillemin, groups all the pathogens which do not sporulate into the single genus, *Cryptococcus*. Castellani [2] in his Milroy lectures has outlined a classification on a strictly morphologic basis. By that also this cerebrospinal blastomyces falls into the genus *Cryptococcus*. The absence of ascus production eliminates both the saccharomycetes and endomycetes from consideration. Monilia exhibits mycelial forms much more constantly than does our cerebrospinal specimen, and also develops chains of cells; it is therefore easily excluded. Torula and mycoderma are characterized, among other things, by the development of a slimy scum in culture which was never present in fluid cultures of our organism.

Guilliermond describes no species which coincides exactly with our specimen. It is true that his work was mostly concerned with such industrial yeasts as interest the brewer and baker; yet there is a fairly full section devoted to pathogenic forms. The medical literature contains more or less full descriptions of blastomyces which are parasitic in the human cerebrospinal axis, and these require the most careful comparison with ours. For the most part, however, the cultural reports are incomplete or inconclusive. Five samples of blastomyces from the central nervous system have been described with sufficient detail to justify analysis.

*Swift and Bull's Case.*—The organism grown by these authors appeared and behaved similarly to ours. Primary cultures were obtained only on Loeffler's blood serum and developed slowly; subcultures grew freely and became yellow with age. No fermentation tests were recorded. They described an encapsulated form which was seen only in the spinal fluid, and not in cultures or sections. The capsule was certainly inconspicuous and was not specifically investigated. A second important difference was in the matter of mycelia. We saw them in one culture tube only, and that was a subculture; Swift and Bull found them only in primary culture. Otherwise, the microscopic appearance tallied with that of our organism. Their organism, however, was not intracellular and did not form cysts.

*Benda's Yeast.*—The cultural data given were very limited and concerned almost exclusively the acid requirements. Glucose was never split. It was an obligate aerobe, and was unable to grow at the bottom of bouillon tubes. Morphologically, the author describes the yeast only in tissue. He does not mention ascus production nor a mucinous envelope.

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2. Castellani, Aldo: J. Trop. Med. **23**:101 (May) 1920.

*Türk's Yeast.*—The characters of this yeast were most minutely described. Microscopically the cells were identical in appearance with ours, and this is well brought out in excellent illustrations. In culture likewise, the two yeasts behaved alike; they grew freely and became yellow. For our purpose, the differences are more useful.

They are: (1) Türk's yeast, unlike ours, developed peripheral translucent wedges (Zwickel). Our variety was grown in company with thirteen other species, during a period of over a year. We made numerous subcultures on different mediums. Other species developed the wedges but they never appeared in the tubes or plates of our yeast. (2) Our yeast frequently became deep orange-yellow in color.

*Flu and Woensdreght's Yeast.*—This organism had the same characters as ours both microscopically and culturally, except that the primary cultures grow on Sabouraud's medium. These authors report that their organism developed no spores (or asci) in special tests. There was no fermentation of glucose, saccharose or mannite.

*Williams' Yeast.*—This author speaks of the lesions in his case as abscesses but he does not mention that the fluid was purulent, nor that leukocytes featured in the histologic sections. We presume, therefore, that the lesions were really cysts. Cultural studies did not include the use of solid sugar mediums, so that there was no opportunity for the yellow color to develop; but a leaning in that direction is indicated by the yellowish white color of plain agar cultures. This organism appears to have been identical with ours except that growth of his cultures was inhibited at room temperature. Williams emphasizes the stickiness of the growth and observed mycelia in the kidney of an inoculated rabbit.

*Frothingham's Yeast.*—Stoddard and Cutler did not secure cultures from their two patients, but they restudied Frothingham's material from a horse, and their very full description leaves no doubt that our organism was the same as Frothingham's. The only points that we wish to restate are that no sliminess or pellicles developed in their fluid mediums, and that they mention no intracellular fat bodies; both of these are usual in the *Torulae* in which they place their organism. The mucinous envelope around the cells was observed in culture, and unlike ours, became stained with methylene blue, Wright's, and Giemsa's stain.

These same authors are responsible for the name *"Torula histolytica"* which we have accepted for our yeast; they applied it, we assume, both to the organisms of the human cases, and to Frothingham's horse cultures. In placing this yeast in the genus *Torula,* they devote no special paragraph to the diagnosis of the established genus

*Torula Turpin* and its comparison with the characters of their yeast. Clearly, their comparative table is directed at the three classes of yeast *infection* that they studied and not at any taxonomic divisions of the microorganism. We take it therefore, from sentences scattered through the text, that they have cut the Gordian knot and have placed the yeast in the *Torulae*, more on the basis of the type of disease produced (influenced by Wolbach), than in conformity to the usual procedures of the general biologist. On the basis of the latter we feel that the name *Cryptococcus histolytica* would be more correct; nevertheless we accept the name *Torula histolytica* for our organism, not so much on the ground of its appropriateness as to avoid adding to the confusion of a frontier subject like yeast classification.

After reviewing the seven yeasts that have been cultured (including the one here reported), the question arises as to which were *Torula histolytica*. Two are so fully described as to permit us to say that this organism can be incriminated in Frothingham's and Flu and Woensdreght's cases as well as our own.[3] The cases of Stoddard and Cutler are not acceptable as they did not grow the organisms; an identical appearance of the yeast in the tissue and identical effect on the tissue do not guarantee that the same microorganism is at work. Türk's data are so complete as to differentiate his organism from *Torula histolytica*. The remaining cases of Swift and Bull, Benda, and Williams are doubtful. But there can be no doubt that several, at least, of these and the cases without cultures were caused by *Torula histolytica*.

### ANIMAL INOCULATION EXPERIMENTS

When guinea-pigs were inoculated intraperitoneally with spinal fluid or fresh cultures they lost weight rapidly and died in from four days to two weeks, without specific alterations in the brain or other organs. As a rule we were unsuccessful in recovering the organisms by culture or smears, and none were found in the sections. Inoculated intranasally, the period of infection lasted from two to three weeks and at necropsy the organisms were demonstrable by smear and culture from various organs, and by histologic examination in the cerebral meninges.

The only successful reproduction of the cystic disease took place in a guinea-pig which was injected subcutaneously. Six months later the animal was found dead in its cage. The testes were greatly enlarged and broken down; and sticky, yellow pus was being discharged from several sinuses. Grossly, the internal organs appeared normal and were not examined histologically. No abnormality was noted in the fresh

3. Frothingham's yeast was obtained from the lung of a horse; there are, therefore, only two cystic brain cases for which the responsibility of this organ is established.

brain but, on histologic examination, numerous multilocular cysts containing yeast cells were found, which corresponded almost exactly with the condition in the human brain. In the guinea-pig there was a moderate, perivascular, round-cell infiltration, which the human case did not show, but the formation of giant cells was similar. Examination of the testes revealed invasion of the gland here and there by organisms; in the subcutaneous tissue there were multilocular cysts of large size, which gave the whole area a reticulated appearance. In these cysts there were yeast cells, both free and in phagocytes, just as in the brain. Flu and Woensdreght, Evans,[4] and Stoddard and Cutler[5] reported similar results, and Klarfeld[6] had produced cystic infiltration of the cerebral gray matter in dogs with a different organism.

## FREQUENCY

Cystic infiltration of the gray matter similar to that described here has been recorded by Zenker,[7] von Hansemann,[8] Benda,[9] Flu and Woensdreght,[10] Riley and L$_e$ Count,[11] Rusk and Farnell[12] (two cases), Williams,[13] Stoddard and Cutler,[5] and Pierson.[14] All of these authors emphasized the irregular distribution of the cysts, their limitation to the gray matter and the absence of tissue reaction. Giant cells are mentioned in several reports, although Rusk and Farnell believed them to be mere zoogleal masses of the organisms. Other authors have

4. Evans, Newton: Torula Infection, California State J. of Med. **20**:383, 1922.

5. Stoddard, J. L., and Cutler, E. C.: Torula Infection in Man, Monograph No. 6 from the Rockefeller Institute for Medical Research, New York (Jan. 31) 1916.

6. Klarfeld: Zur Histopathologie der experimentalen Blastomykose des Gehirns, Ztschr. f. d. ges Neurol. u. Psychiat. **58**:176, 1920.

7. Zenker: Encephalitis mit Pilzentwickelung im Gehirn, Jahres. d. Gesellsch. f. Natür. u. Heilk. in Dresden, 1861-1862, p. 51.

8. Von Hansemann: Ueber einen Fall von Hefenerkrankung, Centralbl. f. allg. Path. u. path. Anat. **16**:347 (July 1) 1905.

9. Benda: Ein Fall von Blastomykosis Cerebri, Deutsch. med. Wchnschr. **33**:945, 1907.

10. Flu and Woensdreght: Een Geval Blastomycose van het Centraalzenuwustelsel, Meded. v. d. burgerl. Beneesk. dienst. in Nederl. Indie **6**:1, 1918.

11. Riley, F. B., and LeCount, E. R.: A Case of Systemic Blastomycosis, Arch. Int. Med. **13**:614 (April) 1914.

12. Rusk and Farnell: Systemic Oidiomycosis. A Study of Two Cases Developing Terminal Oidiomycetic Meningitis, Univ. California Pub. Pathology **2**:47, 1912.

13. Williams, J. R.: A Case of Systemic Blastomycosis, M. J. Australia **2**:185, 1922.

14. Pierson, P. H.: Torula in Man, J. A. M. A. **69**:279 (Dec. 29) 1917.

described lymphocytes and plasma cells about the cysts and in the meninges, and Zenker and Williams described the cysts as small abscesses.

It is a question whether the cysts are formed by internal expansion of the proliferating organisms, or by lysis of tissue due to the specific biologic activity of the organisms. Stoddard and Cutler believed the latter and named the organism *Torula histolytica* on account of this supposed action. We are not satisfied that this is entirely the case. In the first place the surrounding tissue shows evidences of compression. In the second place the septa are formed by well preserved nervous tissue; thirdly there is not enough fatty material in the cysts and their vicinity and about the vessels to point to active destruction; and lastly the organism when grown on fresh sterile brain, produced no solution of the medium.

Cases of meningitis without cyst formation have been reported by Türk,[15] Swift and Bull,[16] Versé,[17] Goto,[18] and Tedesko,[19] in the case of Curtis[20] and the two cases reported by Evans no necropsy was made. These cases are included in order that diffuse blastomycosis of the central nervous system may be better understood.

In these twenty cases (which include that here reported) of diffuse meningeal blastomycosis no extracranial lesion was found in five cases. In the cases of Zenker, Flu and Woensdreght, and Türk, exudates containing blastomyces were present in the pharynx. In Stoddard and Cutler's Case 1, there was an exudate in the pharynx that was not examined. Five patients presented lesions in many organs, and five had pulmonary involvement.

### PORTALS OF ENTRY

The cases of predominant or "primary" blastomycosis of the central nervous system are of special interest on account of the question of the portal of entry. The pharyngeal exudates in the cases of Zenker, Türk, and Flu and Woensdreght may have been terminal, for they appeared shortly before death. Moreover, Flu and Woensdreght, after intracardiac injection of the organism, recovered it from the nasal cavity as well as from the brain. The lung is certainly one portal of entry; not only are five cases reported in which there was coincident

15. Türk: Ein Fall von Hefeinfektion (Saccharokykose) der Meningen, Deutsch. Arch. f. klin. Med. **90**:367, 1907.

16. Swift and Bull: Blastomycotic Meningitis, M. J. Australia, **2**:265, 1917.

17. Versé: Ueber einen Fall von generalisierten Blastomykose beim Menschen, Verhandl. d. deutsch. path. Gesellsch. **17**:275, 1914.

18. Goto: Ueber Blastomycetenmeningitis, Mitt. a. d. med. Fak. d. k. Univ. Tokyo **15**:75, 1915.

19. Tedesko, quoted by Helly in Discussion on Versé (Footnote 13).

20. Curtis: Presse méd., 1895, p. 370.

pulmonary involvement, in addition to five with generalized blastomycosis, but in three cases ulcerative tuberculosis was found, in one bronchiectasis, and in another residual influenza. Thus in fifteen of the twenty cases, the lungs were diseased. The alimentary tract forms another possible portal of entry. Tanaka [21] recently reported the isolation of several species of blastomyces from the mesenteric nodes of persons who had died from various diseases. We obtained our organisms from a peripancreatic lymph node. In our case the portal of entry may have been the tonsils, for the cervical lymph nodes became enlarged after tonsillectomy, and one of these nodes, when excised five years later, presented appearances not unlike those found in the axillary and mesenteric lymph nodes at necropsy.

## SUMMARY

1. We report a twelfth case of cystic infiltration of the cerebral gray matter with a blastomyces.

2. The clinical picture is that of tuberculous meningitis or unlocalized brain tumor, but the organisms are readily found in the spinal fluid.

3. The organism in our case was *Torula histolytica* Stoddard and Cutler.[22]

4. The route by which the brain becomes infected is in doubt.

5. The organism excites hyperplasia of the meninges and the formation of phagocytic giant cells. It provokes no reaction either of neuroglia or connective tissue elements in the cerebral substance, and causes no infiltration with leukocytes. It forms cysts in the cerebral gray matter by internal expansion and exudation. It probably travels along the perivascular lymph spaces.

6. The disease was transmitted to guinea-pigs. These developed a general infection, and, in one animal, there was cystic infiltration of the brain and testes.

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21. Tanaka: Saccharomyces in Mesenteric Glands of the Human Body, J. Path. & Bacteriol. **23**:350, 1920.

22. Cultures of *Torula histolytica* have been deposited in the National Collection for Type Cultures, Lister Institute, Chelsea Gardens, London. Culture and histologic sections have been deposited at the Army Medical Museum, Washington, D. C.

# EXPERIMENTAL CONVULSIONS

## A CONSIDERATION OF THE EPILEPTOGENOUS ZONES OF THE CENTRAL NERVOUS SYSTEM *

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Since the discovery by Fritsch and Hitzig [1] of the electrical irritability of the brain, numerous theories concerning the site of convulsive discharge have been proposed. It is unfortunate that the site of the convulsive discharge has been considered inseparable from the pathology of the disease, epilepsy. It is further unfortunate that much of the work has been concerned with the establishment of a so-called convulsive center. These conditions are in part responsible for the existing confusion relating to the pathogenesis of epilepsy.

Kussmaul and Tenner [2] in 1857, succeeded in producing convulsions in rabbits as the result of cerebral anemia. They were further able to evoke such convulsions after removal of the cerebrum, and pointed out the importance of the brain stem in the production of the convulsion. Nothnagel [3] then localized a special convulsive center in the pons and medulla. It was pointed out by Bubnoff and Heidenhain [4] that both cortical and subcortical lesions are concerned in the production of a convulsion. Upon experimental grounds Ziehen [5] proposed that the clonic component of the convulsion was purely cortical, whereas the tonic component was of subcortical origin. He showed that, when, in the presence of a tonic-clonic convulsion, the cortex was extirpated, the clonic element disappeared. It was possible for Binswanger [6] to produce convulsive attacks by irritation, electrical or mechanical, of the pons, but the attacks were tonic in nature.

The production of convulsive seizures by electrical irritation of the cortex then brought the cortical theory of convulsions to the foreground.

It is apparent therefore, that there are three chief theories as to the location of the convulsive site: First, that which deals with the cortex alone (Hitzig and Fritsch, Luciani, Unverricht, and others);

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* From the Nelson Morris Memorial Institute for Medical Research of the Michael Reese Hospital and Northwestern University Medical School.

* Read at the Third Annual Meeting of the Association for Research in Nervous and Mental Diseases, Dec. 28, 1922.

1. Fritsch and Hitzig: Archiv. f. Anat. u. Physiol. p. 300, No. 2, 1870.
2. Kussmaul and Tenner: London, New Sydenham Society, p. 105, 1859.
3. Nothnagel: Virchow's Archiv. **44**:1, 1868.
4. Bubnoff and Heidenhain, R. P.: Pflüger's Archiv. **26**:137, 1881.
5. Ziehen, Theodore: Archiv. f. Psychiat. **17**:99, 1886.
6. Binswanger: Archiv. f. Psychiat. **19**:759, 1887.

second, the combined cortical and subcortical theory (Ziehen, Bubnoff and Heidenhain, Binswanger, Hughlings Jackson, and others); and, third, the medullary theory (Kussmaul and Tenner, Van der Kolk, Nothnagel, and others).

The experiments in support of these theories have been of two types: first, those in which convulsive seizures have been produced by irritation (mechanical, chemical or electrical) of various parts of the central nervous system; and, second, those in which experimentally produced convulsions have been modified or stopped by ablation of certain parts of the central nervous system, or their occurrence has been prevented by such ablation (excision, separation, freezing, and cocainization).

The proponents of the medullary theory have assumed that if convulsions may be produced by irritation of the pons and the medulla, and may occur as the result of intoxication with absinthe, etc., in decerebrated animals, the convulsive site is located in the pons and medulla, or the pons and medulla possess epileptogenous properties. Opposed to this are the observations: that when a convulsion occurs as the result of irritation of the pons, the clonic element disappears after the removal of the cerebrum (Ziehen, Bechterew, Lewandowsky); that when the cerebral hemispheres are extirpated, it is impossible to produce a convulsion possessing tonic and clonic elements; that when convulsive seizures are produced by toxins, such as absinthe, the clonic element of the attack disappears after the removal of the motor cortex (Borischpolsky and Ossipow); and that removal of one cerebral hemisphere causes the convulsions to disappear from one-half of the body. The observations relative to toxic convulsions are not unchallenged, as Albertoni [7] was able to produce in dogs, after full recovery from a section below the optic thalami, a generalized bilateral convulsion by the use of cinchonidin. Grünwald [8] observed typical picrotoxin convulsions in a decerebrate cat and dog, and subsequent workers have made similar observations.

The proponents of the mixed theory are dependent upon observations of certain motor manifestations produced by stimulation of various parts of the central nervous system. Many of these experiments have nothing to do with convulsions. They are concerned with the production of certain forced movements, ataxia and dystonia; included among them are the experiments of Flourens, Schiff, and Majendie on the quadrigeminal bodies, of Nothnagel, Albertoni, Michieli, Lussana and others on the basal ganglions.

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7. Albertoni: Archiv. f. exper. Path. u. Pharmakol. **15**:258, 1882.
8. Grünwald: Archiv. f. exper. Path. u. Pharmakol. **60**:249, 1909.

The evidence which has supported the theory of the cortical origin of convulsive seizures has been supplied chiefly by the observation of convulsions produced by electrical stimulation of the cortex. Here it has been found that convulsions may be produced which resemble epilepsy, (Fritsch and Hitzig, Unverricht, Ferrier and others). It has been shown that if electrical stimulation of the motor cortex is long continued, the resulting isolated contractions of muscle groups become successive and spread to muscle groups innervated by adjacent cortical areas; then they spread to the opposite side, involving, usually, the posterior extremity first, then the anterior extremity and then the face, although variations occur. The resulting convulsion outlasts the electrical stimulation. It has been shown: that if one quickly extirpates an irritated zone the convulsion is inhibited; that after deep decortication, such convulsions cannot be produced; that when certain motor areas have been removed, the movements represented by such areas are absent in an ensuing convulsion; and that the spread of a convulsion may be stopped by deep incisions into adjacent areas of the cortex. Convulsions can be produced not only by irritation of the motor cortex but also by irritation of other cortical areas, for example the occipital region.

It may be assumed to be essential that the cerebral cortex be intact for the production of a cortical fit. Granting that convulsions may be produced by irritation of the cortex, can they be produced by irritation of the subcortical regions? It has been contended that pontine hemorrhage has never produced convulsions and that spontaneous convulsions never occur in decerebrate animals. Luce[9] has observed the occurrence of convulsions in pontine hemorrhage and stated that such convulsions are produced by irritation of the motor field of the pons, because they occurred in his case when connections with the cerebral cortex were destroyed by hemorrhage. He believes that the ganglion cells of the pons possess epileptogenous qualities, and that in man it may be proved that, in addition to cortical epilepsy, a subcortical type exists. He stated, however, that, in his opinion, the pons plays only a secondary part in genuine epilepsy. Rothmann[10] has reported the occurrence of spontaneous convulsions in a decerebrated dog, three months after the operation. The convulsive seizure was tonic in the extremities and clonic in the face. This observation likewise points to the epileptogenous quality of the brain stem. From these observations and from the accumulated experimental work it may, I think, be admitted that, whatever element of a fit may be lacking in a convulsion produced in an animal with a mutilated brain, convulsions, tonic,

9. Luce: Deutsch. Zeitschr. f. Nervenheilk. **15**:327, 1899.
10. Rothmann: Neurol. Centrbl. **31**:1286, 1912.

clonic, or both, may be produced from the cortex and from the subcortical regions; and in the latter case, in the absence of the motor cortex. It may further be admitted that the symptoms of a convulsion vary with the state of preservation of the brain; if it be intact there are: tonic-clonic convulsions associated with sialorrhea, pupillary changes, bladder contraction, circulatory and respiratory changes, and at times an aura.

The aura is dependent on the area of brain irritated, and in Jacksonian epilepsy, as in artificially produced cortical fits, motor movements constitute the aura. In other cases vagal auras exist, or respiratory or circulatory changes precede the convulsion; the portion of the brain here irritated must be at a lower level. It may be pointed out that not only is the tonic element of an epileptic fit absent in a cortical fit, but that loss of consciousness does not occur until a generalized convulsion ensues; involuntary urination does not occur before the loss of consciousness.

An epileptic convulsion consists not only of tonic and clonic movements, but also of a series of events and changes that include the aura, vascular, respiratory and secretory changes, and contraction of the involuntary muscles of the bladder. It has been shown that by irritation of certain parts of the cortex many of these changes may be produced: pupillary changes (Lewandowsky), bladder contraction (Bechterew), circulatory and respiratory changes (Landois), and secretory changes of the salivary glands (Kulz and Braun). These regions are rather widely separated from each other and if it could be shown that all of these changes can be evoked from some relatively small point, their occurrence in epilepsy might be more readily explained. It has been pointed out by Hirt that such symptoms occurring in an epileptic attack have never been adequately explained.

Certain toxic convulsions have thrown some light on this question. The occurrence of convulsions produced by toxic substances in decerebrate animals has been described by Roeber,[11] Perrier,[12] Grünwald and others; who worked with picrotoxin; Albertoni with cinchonidin; Ossipow with absinthe; and others with various substances such as toxiresin, digitaliresin, coriamyrtin, senso, etc. Not only do these substances produce convulsions which, whatever be their pattern, occur after decerebration, but, as was pointed out by Grünwald,[13] they also produce a marked effect on the central autonomic nervous system. He remarked that a review of the literature showed that, in addition to the production of convulsions and injury to the heart muscle, picrotoxin caused: contraction of the pupils (Falck, Roeber, Luchsinger, Perrier);

11. Roeber: Archiv. f. Anat. u. Physiol. p. 38, No. 1, 1869.
12. Perrier: Archiv. f. exper. Path. u. Pharmakol. **4**:191, 1875
13. Grünwald: Archiv. f. exper. Path. u. Pharmakol. **15**:258, 1882.

salivation (Falck, Roeber, Luchsinger, Gottlieb); slow pulse (Roeber, Perrier, Luchsinger, Gottlieb); and urinary bladder contraction (Falck and Gottlieb). He verified these findings and demonstrated the central action of the poison as follows: after cutting the bladder nerves no contraction occurred following the administration of picrotoxin. In a decerebrate cat that had been poisoned with picrotoxin and showed a vagus pulse, salivation and bladder contraction, these three symptoms disappeared on section of the vagus, chorda tympani and pelvic nerves respectively; the symptoms did not recur on further administration of picrotoxin. After section of the right chorda tympani, following the administration of picrotoxin, there was profuse secretion from the left salivary duct but none from the right. From these experiments he concluded that picrotoxin is a poison that acts on the central autonomic nervous system. It can readily be seen that picrotoxin may produce convulsions through action on the medulla and at the same time produce a group of symptoms referable to the central autonomic nervous system, which regularly occur in conjunction with an epileptic convulsion.

With W. L. Treadway [14] I pointed out that certain circulatory and respiratory changes occurred in relation with an epileptic convulsion. We found that in a case of petit mal remarkably well suited for continuous tracings, there was a preliminary rise in blood pressure twenty-six to sixty seconds before the convulsion; when the rise took place more than thirty seconds before a convulsion, the blood pressure usually fell again to a slight degree. Preceding the convulsion by from nine to twelve seconds, there was a sudden marked drop in blood pressure which remained relatively low during the time occupied by the petit mal attack. The aura followed the blood pressure change. A period of apnea preceded the convulsion or its equivalent by from four to nine seconds.

Knauer [15] has observed inhibitory spasm of respiration in the beginning of an epileptic attack which he attributed to spasmodic closure of the glottis. In reviewing the work of Treadway and myself, I was astonished that the obvious fact that apnea occurred in inspiration escaped our notice. The apnea certainly was not due to closure of the glottis, which would not interfere with movements of the chest, yet this observation makes it necessary to show that the apnea is not the result of the tonic element of the fit. I have been fortunate in obtaining a series of tracings of the respiration and blood pressure of a girl in status epilepticus. In these it can be seen that, preceding the convulsion, there was a cessation of respiration in the expiratory phase

14. Pollock, L. J., and Treadway, W. L.: Arch. Int. Med. **12**:445, 1913.
15. Knauer: Zeitschr. f. d. ges. Neurol. u. Psychiat. **3**:625, 1910.

with a few very ill-defined movements of the chest wall and then an inspiratory spasm. Unfortunately, the blood pressure curve was valueless because of a defect in the Erlanger valve. It may be well to point out that in picrotoxin convulsions the apnea sometimes occurred at a point midway between inspiration and expiration and usually in expiration. Although Grünwald attempted to show that the blood pressure changes were due to respiratory embarrassment, we have pointed out that the rise and fall of blood pressure at times occurred independently of the period of apnea. At times respiration may only be diminished, no period of apnea being present; and at other times respiration may actually be increased, and blood pressure variations may occur. I feel, therefore, that the circulatory and respiratory changes occur as the result of medullary stimulation and not as the result of muscular movement or respiratory embarrassment.

From the facts that respiratory and circulatory disturbances preceded the convulsion or equivalent, the conclusion was reached that in some cases of petit mal the site of discharge is in the medulla and pons.

If convulsions which are caused by discharge in the medulla and pons are accompanied by a train of circulatory and respiratory symptoms, it would seem likely that these symptoms should be present in a medullary convulsion artificially produced.

W. H. Holmes and I [16] studied respiration and circulation in picrotoxin convulsions and found that a period of apnea occurred with the convulsion; it usually began with the severe clonic seizure, but sometimes followed it. We likewise found that there was a periodic rise and fall in blood pressure as part of the manifestation of picrotoxin poisoning; this took place about the time of the convulsion but without having a definite relation to it, or being caused by it or the period of apnea. Similar circulatory changes occurred in a decerebrate animal. It was found that although apnea and blood pressure changes occurred with the convulsion caused by picrotoxin, they did not bear the same constant relation to the convulsion as was found in the case of petit mal. From the facts that there exist medullary convulsants and that the convulsions which they produce are associated with symptoms referable to the central autonomic nervous system similar to those found in idiopathic epilepsy, and with circulatory disturbances analogous to those found in idiopathic epilepsy, we concluded that we had further evidence that the site of discharge of the convulsion in some types of idiopathic epilepsy is in the medulla and pons. The medulla and pons participate in the convulsion in all cases of epilepsy, whether the site of discharge is there or not.

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16. Pollock, L. J., and Holmes, W. H.: Arch. Int. Med. **16**:213, 1915.

It has become necessary to define what is meant by "site of discharge." By this term is meant that area of the central nervous system which, because of stimulation of a certain character, evokes the beginning of a convulsion. It does not signify a special center for convulsions, but only that such an area possesses epileptogenous quality. With this in mind, it appears to me just as logical to assume in those cases in which the first sign of convulsion may be referred to the central autonomic nervous system, that the irritation producing the convulsion is first expended upon the brain stem, as it is to attribute the origin of Jacksonian fits to the cortex. The objection of the proponents of the cortical theory of epilepsy, that in subcortical fits the clonic element is absent, would, even if it were true, be equivalent to the objection that in a cortical fit the tonic element, which is always observed *first* in an epileptic convulsion, is absent.

In the present work which, unfortunately, is limited, it was proposed to determine whether, in picrotoxin poisoning, an isolated segment of the brain stem could evoke convulsive seizures in the muscles innervated by this segment.

Twenty-eight animals, eight cats and twenty dogs, were studied, and a large number of frogs were observed under certain conditions. Of the cats and dogs, ten animals afforded successful experiments. Of these, three were decerebrated by a transection of the brain stem below the optic thalami; four by transection immediately below the level of the nucleus of the seventh cranial nerve; and three were transected at two levels, one below the optic thalami and the other immediately above the level of the nucleus of the seventh cranial nerve. Of the last group, one received a hypodermic injection of picrotoxin solution following the section in the pons above the seventh nerve. The other two received the injection following the double transection.

The section above and below the level of the seventh cranial nerve was performed by two methods, the first having an approach through a cerebellar decompression opening, and the other through the sphenoid bone in the roof of the mouth. A satisfactory technic was developed by both methods. Intratracheal artificial respiration was employed and ether used as an anesthetic. The dose of picrotoxin employed was about eight milligrams per kilogram of body weight of the animal.

As had been observed before, it was readily seen that a number of factors were responsible for differences in the pattern of convulsive movements; shock, hemorrhage, degree of respiratory failure, degree of postoperative recovery, the manner in which the anesthetic was taken, the duration of the operation, were all factors which could not be accurately controlled; therefore convulsive seizures frequently differed in type, although the procedures were apparently the same.

In two of the three animals with a section below the optic thalami, convulsions were produced that differed in no discernible way from animals with intact central nervous systems. The muscles of the face, jaw, and eyeballs participated in the convulsion. In the remaining animal the convulsions were tonic in character and were followed by running movements. Convulsive movements occurred in the face, jaw and eyeballs as in the other two animals.

It was observed that when a section was made at lower levels in the brain stem, convulsions were produced with greater difficulty; they required at times twice the amount and occasionally even more than twice the amount, of picrotoxin solution. When convulsions were produced, their intensity was far less than those produced in animals in which higher transections had been made. In two of the four animals transected immediately below the level of the nucleus of the seventh cranial nerve, a generalized picrotoxin convulsion was produced. In one of these the muscles of the jaw, face and eyeballs participated in the convulsion. Of the three animals transected at two levels, the animal which received a hypodermic injection of picrotoxin solution following the section immediately above the level of the seventh nerve, developed a typical picrotoxin convulsion with strong clonic contractions of the masseters and of the muscles of the eyeballs. When this animal's brain stem was transected again below the level of the optic thalami, the convulsions became less pronounced, but retained clonic and tonic features, though the movements of the jaw and eyeballs ceased. The remaining two animals did not develop any convulsion after the double transection.

From these animals it will be observed that picrotoxin convulsions can be produced after transection of the brain stem either below or above the optic thalami, or below the level of the seventh cranial nerve, and that these convulsions retain their clonic features. Whether the animal is transected at one or the other level, some muscles of the head and eyeballs participate in the convulsion. In other words, whether the segment innervating the muscles of the face, jaws and eyeballs was connected with the medulla alone or the cerebrum alone, convulsive disorders occurred in these muscles. It seems probable, although not absolutely proved, that this observation indicates the epileptogenous quality of the motor cells in the reticular formation extending from below the optic thalami to the spinal cord. Although it is true that facial movements and ocular movements ceased after complete isolation of such a segment, it could not be shown that the fifth and seventh nerves were uninjured, inasmuch as the conjunctival reflex did not return.

In ten of the frogs I was able to isolate a segment between the optic thalami and a level below the seventh nerve and was able to

produce picrotoxin convulsions with movements of the jaw and of the eyeballs. The movements of the eyeballs in this animal may, however, have been due to respiratory efforts and therefore may not be the result of a convulsion.

It appears that in a frog the jaw participates in a convulsive seizure when the brain stem, from which the fifth nerve originates, has been separated from the rest of the central nervous system. In higher animals, although the influence of the cortex could not be excluded, it seemed probable that epileptogenous qualities existed in the segment that extends from below the optic thalami to the seventh nerve. It was certainly clear that that part of the medulla from the seventh nerve to the spinal cord possessed epileptogenous qualities.

An attempt was made to find a central autonomic nervous system depressant. The only substance to which such a character has been attributed was botulinus toxin. Although animals receiving this toxin, after a period of incubation, which by the administration of large doses was reduced to eight hours, showed very marked respiratory difficulty followed by ataxia and paresis of extremities, the injection of picrotoxin almost always produced picrotoxin convulsions and respiration was in no way affected. It is doubtful whether botulinus toxin is a true central autonomic nervous system depressant.

## CONCLUSIONS

From these experiments no conclusive evidence could be adduced that an isolated segment of the brain stem contained epileptogenous elements. It appeared highly probable, however, that such was the case.

It would seem that epileptogenous qualities are possessed by the ganglion cells both of the brain and the brain stem; that convulsive movements may be evoked by proper stimulation of such cells at any level; and that the first symptom produced depends upon the level so stimulated.

# STUDIES ON EPILEPSY

## I. CONVULSIONS EXPERIMENTALLY PRODUCED IN ANIMALS COMPARED WITH CONVULSIVE STATES IN MAN

### A PRELIMINARY REPORT *

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Several years ago, a group of physicians under the leadership of Dr. Frederick Tilney, made a critical study of the literature of epilepsy. Frequent meetings were held, and the published papers on the subject were reviewed and discussed. The more the literature was studied, the clearer it became that the nature and cause of the symptoms we call epilepsy, were lost in a maze of theories and contradictions, and that, as a basis for advance, careful research into the causes, nature and site of convulsions was necessary. Only when this is done shall we have a real basis for biochemical research and for logical clinical investigations into the etiology of epilepsy.

With this conclusion came the conviction that the investigation must begin with the simplest problems of the convulsive attack, and gradually advance to the more complex. The following report represents the work along these lines thus far done, but we have touched only the surface of the investigation.

Convulsions in animals can be produced in a variety of ways. After a critical review of previous methods we selected two: first, the injection of essence of absinth (*cultivée*) which was first used by Ossipow and later by many investigators. The second method has, to our knowledge, never before been used for the study of convulsions in animals.[1] We have used methods for the production of convulsions which are perhaps genetically similar to what occurs in man in the convulsive attacks that have a primary toxic or vascular cause. This

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1. We attempted also to use other toxic substances, such as oil of cloves, for injection into the circulation. Our results were inconstant. We have tried to cause uremic convulsions in cats by total or subtotal double nephrectomy, but the results thus far have been negative. Finally we have begun to study the convulsions of asphyxia.

was done because of a certain inherent probability that the ultimate mechanism, and the final pathway of many and perhaps all convulsive attacks in man, no matter what the primary cause or what the disease with which they were associated, were the same.

## EXPERIMENTAL METHODS

The experiments were made on adult cats, and, unless otherwise mentioned, the animals received no food for twenty-four hours before they were used.

A. *Injections of essence of absinth into the femoral vein.*—When essence of absinth (*cultivée*) is injected into the circulation, one or more severe convulsive attacks follow. The convulsions begin abruptly a few seconds after the drug has been injected. There is usually a tonic phase, of short duration, with opisthotonus and retraction of the head, quickly followed by severe clonic convulsions which involve all of the muscles of the body. The convulsions last from one to five minutes, during which the pupils are widely dilated, the corneas are insensitive, respiration is stertorous, and the mucous membranes are cyanotic. Urine is usually expelled and sometimes feces are evacuated. For the ensuing five to ten minutes, there are frequent coarse twitches of the muscles of the trunk and extremities, and sometimes a short period of rigidity of the fore and hind limbs that reminds one of the decerebrate rigidity of Sherrington. After the convulsions have ceased, the animal lies quietly for a time and then sits up and later walks around. Many of the animals, when they first stand up, remain in a fixed position, as if they were afraid to move a single muscle. There may be more than one of the convulsive attacks.

The strength of the solution and the amount to be injected was arrived at only after considerable experimentation. At first we used pure essence of absinth for the injections; later, an emulsion of one part of essence of absinth in twenty of Ringer-Locke solution, of which 0.1 cubic centimeter per pound of animal was injected. We finally found that a solution of one part of essence of absinth in nineteen parts of 95 per cent. alcohol was a useful standard solution with which more exact dosage was possible.[2] Thirty-five thousandths to 0.05 c.c. of this 5 per cent. solution of absinth in alcohol, per pound of animal, was injected into a femoral vein, and this amount was found to be what one might call a normal convulsing dose. If less, per pound of animal, was injected, convulsions were rarely produced; at most the animal had a few convulsive twitches. If, on the other

2. In control animals 95 per cent. alcohol was injected intravenously but such an injection of alcohol was never followed by a convulsion.

hand, more than 0.06 cubic centimeter per pound of animal was used for the first injection, the cat often died in the first convulsive attack.

In order to make certain that absinth convulsions were cerebral in origin the cerebral circulation was interrupted in the manner that will be described in method B, and during the period of cerebral anemia, absinth was injected into a femoral vein. No convulsions ever occurred. The proof that absinth convulsions were of cerebral origin was thus definitely established.

B. *Temporary clamping of the innominate and left subclavian arteries.*—This method was suggested by the experiments of Dr. Frank Pike, of the Neurological Department of the College of Physicians and Surgeons, because, in his studies on the respiration, he had observed and reported that convulsions occurred in animals in which he had temporarily shut off the cerebral circulation. We have studied the convulsions caused by cerebral anemia and have developed the method in the manner we shall later describe.

Under intratracheal ether anesthesia, the innominate and left subclavian arteries are exposed and temporary clamps are applied to the vessels, central to the origin of the vertebral arteries. This shuts off all of the blood supply to the brain except an insignificant quantity that reaches the brain through the spinal arteries. In most of the animals the immediate effect of the procedure is the following: A moment after the vessels have been clamped, the animal's body straightens out and respiratory movements cease. The ether anesthesia is at once stopped and artificial respiration begun. This can be easily done with the intratracheal apparatus. During this period of cerebral anemia, the nose and mucous membranes are pallid, the pupils widely dilated, the corneas insensitive, and spontaneous respiratory movements are abolished. Artificial respiration by insufflation of air has to be continued.

When the clamps are removed from the vessels, the nose and mucous membranes become pink again but the pupils remain widely dilated, the corneas insensitive, and respiration is abolished for from five to thirty minutes or more. Finally, the animal begins to make occasional spasmodic inspirations, and, gradually, regular deep respiratory movements are reestablished. The pupils gradually become contracted, and finally the corneal reflexes return. Only then is artificial respiration discontinued and the intratracheal tube removed. We have found that interruption of the cerebral circulation for eleven minutes gave us the best results.

After a period of time, which varied from ten minutes to one hour, tonic and clonic convulsions occur. Stiffness of several or of all of the extremities is first noticed with an increase in the tendon reflexes

of the fore and hind limbs. This is soon followed by tonic and clonic convulsions. The attacks recur a number of times during the period of observation.

We desire here to call attention to the fact that the convulsions are produced, not by the introduction of a drug into the circulation which may affect every part of the body, but by the simple method of shutting off the blood from the brain. The method permitted us also, in a very simple manner, to establish an artificial circulation through the brain, so that we could pass a variety of fluids through the intracranial circulation. All that was necessary was to inject fluid into a carotid artery above the clamps and to drain off the fluid from one of the jugular veins, a ligature having been tied around the animal's neck and all structures excepting the trachea, esophagus, carotid vessels, and vagus nerves being compressed. This ligature prevents the return of the fluid into the general circulation, except for an amount, that cannot be controlled, that is carried off through the veins in the spinal canal. We thus had a cranial organism— a living test tube for the study of the influence of various solutions and various drugs on the brain. We shall recur in another part of this paper to some of the experiments made with an artificial cerebral circulation, especially to those which have a direct bearing on the subject of this paper. At another time, we shall report upon a number of facts of great interest which have to do with the influence of drugs on the cerebral circulation and upon the functions of the brain.

With these two methods, we have made studies on over 300 cats; as many of these died before experiments were concluded, the number on which this paper is based, is 261 cats. The number of actual experiments was, of course, much larger, as many of the animals were used over and over again.

For the sake of brevity, we shall use the term "convulsing agent" whenever we refer to one of the methods we used for the production of convulsive attacks, and the term "convulsing dose" for the minimum procedure which caused a convulsion in our animals, no matter whether we refer to the duration of the cerebral anemia or the amount of the intravenous injection.

## EXPERIMENTAL RESULTS

I. *After one convulsion has been produced, the susceptibility of the brain is much reduced. For the production of a second convulsion the amount of the convulsive agent has to be much increased. In many instances it is impossible to cause a second convulsion no matter how large the "convulsing dose." This increased resistance or diminished susceptibility is probably an exhaustion phenomenon and persists for one to three days, but disappears in less than ten days.*

This series of experiments was made on 42 animals. A convulsing dose of essence of absinth was first injected. Then after intervals which varied from twenty minutes to ten days, the injections were repeated a number of times. In these animals, the intravenous injection of a convulsing dose of essence of absinth was followed, after the expiration of a few seconds, by one or more general convulsions. Occasionally the convulsive attacks began after a somewhat longer period during which the animal showed signs of restlessness. A second injection, given after about twenty to thirty minutes, was not followed by a convulsion, unless the amount of absinth injected was much increased. Even a large dose may not cause a convulsion. The same results were obtained with each succeeding injection. This "refractory" period lasted for several—often for three days, but one week later, the animal's susceptibility was no different from that of an animal that had never received an injection. Some cats are less susceptible to absinth so that the convulsing dose must be larger, and in these animals a convulsion usually followed as soon as a second injection had been given. These animals, also, were thereafter much less susceptible to succeeding injections and their behavior was identical with that of the animals which had a convulsive seizure after the first injection. The explanation for this change in susceptibility is not clear and further investigations along these lines will be made, but, theoretically the phenomenon may be one of exhaustion of some part of the central or peripheral nervous system.

The lack of specific response—a convulsion—to succesive convulsing doses is seen also after the temporary interruption of the blood supply to the brain by the second method we have described above (method B) although its demonstration is difficult. If, after a convulsion has been produced by an intravenous injection of absinth, the brain is deprived of its blood supply for eleven minutes by temporary compression of the innominate and left subclavian arteries, no convulsions follow this latter procedure (see Experiments 123 and 134). In other words, if the animal has had a convulsion from absinth, it is less susceptible, or not at all susceptible, to convulsive attacks from cerebral anemia.

SAMPLE PROTOCOLS FROM THIS SERIES OF EXPERIMENTS

| PROCEDURE | RESULT |
|---|---|
| Cat 126. Weight, 6 pounds. | |
| 1. 0.75 c.c. of 5 per cent. emulsion of absinth in Ringer-Locke solution injected into the femoral vein. | Immediate violent convulsion for five minutes. |
| 2. One hour later: Injection of 1.2 c.c. | No convulsion. |
| Cat 127. Weight, 5 pounds. | |
| 1. 0.5 c.c. of absinth in Ringer-Locke solution injected (0.1 c.c. per pound). | Immediate violent convulsion for five minutes. |

| Procedure | Result |
|---|---|
| 2. Ninety minutes later: Second injection. 1 c.c. (0.2 c.c. per pound). | Delayed convulsion of short duration. |
| Cat 128. Weight, 5 pounds. | |
| 1. 0.5 c.c. (0.1 c.c. per pound) of absinth in Ringer-Locke solution injected. | Immediate violent convulsion for two minutes. |
| 2. Sixty minutes later: Injection of 0.5 c.c. | No convulsion. |
| 3. Thirty minutes later: Injection of 1 c.c. (0.2 c.c. per pound). | Delayed convulsion, not violent nor of long duration. |
| Cat 144. Weight, 7¾ pounds. | |
| 1. Injection of 0.75 c.c. of 5 per cent. solution of absinth in 95 per cent. alcohol. | Violent convulsion for one minute. After three minutes violent convulsion for two minutes. |
| 2. Forty-five minutes later: Injection of 0.4 c.c. | No convulsion. |
| 3. One week later: Injection of 1.5 c.c. | Two violent convulsions. |
| 4. Fifteen minutes later: Injection of 1.5 c.c. | No convulsion. |
| Cat 146. Weight, 8 pounds. | |
| 1. Injection of 0.4 c.c. (0.05 c.c. per pound) of absinth in alcohol. | Immediate violent convulsion. |
| 2. Thirty-five minutes later: Injection of 0.8 c.c. (0.1 c.c. per pound). | Delayed violent convulsion. |
| Cat 148. Weight, 7 pounds. | |
| 1. Injection of 0.35 c.c. (0.05 c.c. per pound) of absinth in alcohol. | Two violent convulsions in close succession followed by many muscular twitches. |
| 2. Fifteen minutes later: Injection of 0.35 c.c. | No convulsion or twitchings. |
| Cat 230. Weight, 8 pounds. | |
| 4:05 p. m.: Injection of 0.24 c.c. of absinth in alcohol (0.03 c.c. per pound). | No convulsion. |
| 4:31 p. m.: Injection of 0.32 c.c. (0.04 c.c. per pound). | Convulsion for two minutes. |
| 4:50 p. m.: Injection of 0.32 c.c. | No convulsion. |
| Cat 233. Weight, 7¼ pounds. | |
| 3:10 p. m.: Injection of 0.29 c.c. (0.04 c.c. per pound) of absinth in alcohol. | Immediate violent convulsion and prolonged muscular twitches. |
| 3:53 p. m.: Injection of 0.29 c.c. | No convulsion. |
| 4:20 p. m.: Injection of 0.35 c.c. (0.05 c.c. per pound). | No convulsion. |
| 4:43 p. m.: Injection of 0.43 c.c. (0.06 c.c. per pound). | No convulsion. |
| Cat 234. Weight, 5¼ pounds. | |
| 3:17 p. m.: Injection of 0.21 c.c. of absinth in alcohol (0.04 c.c. per pound). | Immediate violent convulsion for one minute followed by muscular twitches for fifteen minutes. |
| 4:25 p. m.: Injection of 0.26 c.c. (0.05 c.c. per pound). | No convulsion. |
| 4:46 p. m.: Injection of 0.31 c.c. (0.06 c.c. per pound). | No convulsion. |
| Cat 248. Weight, 5½ pounds. | |
| 3:55 p. m.: Injection of 0.25 c.c. of absinth in alcohol (0.05 c.c. per pound). | Two severe convulsions. |
| 4:10 p. m.: Injection of 0.25 c.c. | No convulsion. |

| PROCEDURE | RESULT |
|---|---|
| 5:15 p. m.: Injection of 0.25 c.c. | Few muscular twitches. |
| Cat 123. Weight, 10¾ pounds. | |
| 1. 0.1 c.c. of essence of absinth. | Violent convulsion for five minutes. |
| 2. Ninety minutes later, clamping of cerebral vessels for eleven minutes. | No convulsion. |
| Cat 134. Weight, 5 pounds. | |
| 1. Injection of 0.5 c.c. of absinth in Ringer-Locke solution. | No convulsion. |
| 2. Fifteen minutes later: Injection of 0.5 c.c. | Violent convulsion. |
| 3. Two and one-half hours later: Clamping of cerebral vessels for ten and one-half minutes. | No convulsion. |

II. *In thyroidectomized animals, the susceptibility to the first injection of absinth is greater than in normal animals, and the susceptibility to repeated injections is completely altered. Each injection of absinth causes a convulsion.*

This series of experiments was performed upon twelve cats in which the thyroid had been completely removed, and which had survived for seven to fourteen days.[3] The experiments demonstrated the remarkable fact that the animals were more susceptible than normal cats to convulsive attacks after the first convulsing dose of absinth, and that they were susceptible to repeated injections, each injection being followed by a violent convulsion and prolonged muscular twitchings. Some typical experiments follow:

| PROCEDURE | RESULT |
|---|---|
| Cat 222. Weight, 5¾ pounds. Thyroidectomy seven days previously. | |
| 2:50 p. m.: Injection of 0.06 c.c. of absinth in alcohol (0.01 c.c. per pound). | Short convulsion after one minute. |
| 3:02 p. m.: Injection of 0.12 c.c. (0.02 c.c. per pound). | Violent convulsion for one and one-half minutes. |
| Cat 223. Weight, 5½ pounds. Thyroidectomy seven days previously. | |
| 2:35 p. m.: Injection of 0.17 c.c. of absinth in alcohol (0.03 c.c. per pound). | Violent convulsion after five seconds. |
| Cat 245. Weight, 5½ pounds. Thyroidectomy twelve days previously. | |
| 2:46 p. m.: Injection of 0.16 c.c. of absinth in alcohol (0.03 c.c. per pound). | Rapid breathing. |
| 3:07 p. m.: Injection of 0.3 c.c. of absinth in alcohol (0.05 c.c. per pound). | Immediate violent convulsion followed by muscular twitches. |
| 3:30 p. m.: Injection of 0.30 c.c. (0.05 c.c. per pound). | Violent convulsion with twitches. |

3. As the parathyroid glands in cats, and the blood vessels which supply them, are very small, we have not yet been able to determine whether all of the parathyroids were injured during the thyroidectomies.

| Procedure | Result |
|---|---|
| 3:50 p. m.: Injection of 0.3 c.c. | Violent convulsion for two minutes. |
| 4:11 p. m.: Injection of 0.3 c.c. | Three severe convulsions followed by muscular twitches. |
| 4:31 p. m.: Injection of 0.3 c.c. | Died. |
| Cat 246. Weight, 10 pounds. Thyroidectomy one week previously. | |
| 2:57 p. m.: Injection of 0.5 c.c. of absinth in alcohol (0.05 c.c. per pound). | Immediate violent convulsion. |
| 3:25 p. m.: Injection of 0.5 c.c. | Violent convulsion. |
| 3:47 p. m.: Injection of 0.5 c.c. | Violent convulsion. |
| Cat 247. Weight, 5 pounds. Thyroidectomy one week previously. | |
| 2:33 p. m.: Injection of 0.15 c.c. of absinth in alcohol (0.03 c.c. per pound). | Two convulsions after two minutes, followed by muscular twitches. |
| 3:12 p. m.: Injection of 0.15 c.c. | Severe twitching of muscles of body and extremities. |
| 3:36 p. m.: Injection of 0.15 c.c. | Violent convulsion. |
| 4:04 p. m.: Injection of 0.15 c.c. | Violent convulsion. |
| Cat 261. Weight, 3½ pounds. Thyroidectomy one week previously. | |
| 12:22 p. m.: Injection of 0.17 c.c. of absinth into femoral vein (0.05 c.c. per pound). | Six violent convulsions with twitches during twenty minutes. |
| 1:47 p. m.: Injection of 0.15 c.c. absinth. | Six violent convulsions during eighteen minutes. |
| 3:02 p. m.: Injection of 0.15 c.c. absinth | Seven violent convulsions during thirty-eight minutes. |

Of the twelve cats used for this series, eight gave positive results; two died after the second injection, and two gave negative results. More than one convulsion after each absinth injection was often seen; one of the animals (Cat No. 261) had six or seven severe convulsive attacks after each absinth injection.

The results of these experiments suggest that the thyroid (and perhaps the parathyroid glands) has a profound influence on the parts of the brain, and possibly of the peripheral nervous system, concerned in the convulsive attacks, and perhaps has significance with respect to the frequency of convulsive attacks in man. It may be that the thyroid (and perhaps other ductless glands) exerts an inhibitory or check influence upon the activity of the cortical and subcortical motor cells and even on other parts of the motor pathways; the experiments just described seem to point in that direction. Lack of thyroid gland activity may play an important rôle in so-called status epilepticus.

We have made some investigations upon the effect of absinth in animals who had received an intravenous injection of thyroid extract. These experiments are as yet few in number, but they seem to indicate that cats who have been given an intravenous injection of thyroid extract, followed by a convulsing dose of absinth, react in the same way as normal animals. We have not yet investigated the susceptibility

of thyroidectomized cats to convulsions from cerebral anemia produced by our method B, nor have we given injections of thyroid extract followed by absinth to cats from whom the thyroid gland had previously been removed. These experiments will be done in the near future.

III. *Diminished alkalinity of the blood does not render cats more susceptible to convulsions produced either by injections of absinth or by cerebral anemia. It is possible, therefore, that the diminished alkalinity of the blood so often found in man before and during an epileptic attack occurs as a result of, or in association with, the convulsive attack, rather than that it favors a convulsive seizure.*

This conclusion was arrived at as the result of experiments on forty-six cats in which the alkalinity of the blood was diminished by means of injections of lactic acid; in many of them this was done before and after convulsing agents were used. The alkaline reserve in the tissues of the body, is continuously yielded to the blood so that the reaction of the blood remains almost constant. When the alkaline reserve has been used up, the blood becomes acid and death at once ensues. A large number of experiments was required before we had determined the amount of acid necessary to overcome the alkaline reserve and reduce the alkalinity of the blood without causing the death of the animal. We finally determined that an injection of 1 c.c. of a 10 per cent. solution of lactic acid, U. S. P., for every pound of animal would reduce the alkalinity of the blood for a short period. The tests were made with the Van Slyke carbon dioxid method, and the Van Slyke apparatus, and the following results were obtained:

Cat 151. Weight, 9 pounds. Under intratracheal anesthesia, 7 c.c. of blood was extracted from a vein and the gas content of the plasma was determined by the Van Slyke method. The reading of the scale was 5. Five minutes later, 9 c.c. of 10 per cent. lactic acid was injected into the jugular vein. Twenty minutes later, blood was extracted and tested. The reading was 4.2.

Cat 152. Weight, 6¼ pounds. The gas content of the blood plasma before the injection at three tests was 5, 5, and 5. The gas content of the blood plasma twenty minutes after injection of 6.25 c.c. of 10 per cent. lactic acid was 4, 4 and 4.2 in three tests.

These experiments demonstrated that the blood alkalinity had been reduced by the amount of acid injected.

We then attempted to learn whether animals, in which the alkalinity of the blood had been reduced, were more susceptible to injections of absinth, so that the convulsing dose could be smaller than in normal cats. As the experiments demonstrate, diminished alkalinity of the blood has no such effect.

| PROCEDURE | RESULT |
|---|---|
| Cat 156. Weight, 5¾ pounds. | |
| 1. Intravenous injection of 5.75 c.c. of 10 per cent. lactic acid (1 c.c. per pound). | |
| 2. One minute later: Injection of 0.28 c.c. (0.05 c.c. per pound) of a solution of absinth 1 part and 95 per cent. alcohol 19 parts. | No convulsion. |
| 3. Forty-five minutes later: Injection of 0.28 c.c. of absinth solution. | Violent convulsion for one minute. |
| Cat 157. Weight, 5½ pounds. | |
| 1. Injection of 5.5 c.c. of lactic acid solution. | |
| 2. One minute later: Injection of 0.27 c.c. of absinth. | No convulsion. |
| 3. Forty-five minutes later: Injection of 0.22 c.c. of absinth (0.04 c.c. per pound). | No convulsion. |
| Cat 159. Weight, 6¼ pounds. | |
| 1. Injection of 6.25 c.c. of lactic acid solution (1 c.c. per pound). | |
| 2. One minute later: Injection of 0.31 c.c. (0.05 c.c. per pound) of absinth. | Delayed convulsion which lasted one minute. |
| 3. Forty-five minutes later: Injection of 0.31 c.c. of absinth. | No convulsion. |
| Cat 161. Weight, 7½ pounds. | |
| 1. Injection of 7.5 c.c. of lactic acid solution. | |
| 2. One minute later: Injection of 0.3 c.c. (0.04 c.c. per pound) of absinth. | No convulsion. |
| 3. Thirty minutes later: Injection of 0.45 c.c. (0.05 c.c. per pound) of absinth. | Two violent convulsions. |
| Cat 186. Weight, 8½ pounds. | |
| 1. Injection of 17 c.c. (2 c.c. per pound) of lactic acid solution. | |
| 2. A few seconds later: Injection of 0.21 c.c. (0.025 c.c. per pound) of absinth. | No convulsion. |

These few experiments, typical of the protocols of many, demonstrate that there is no increased susceptibility to convulsions by absinth when the alkalinity of the blood has been decreased. In fact six of fifteen cats which had received an injection of lactic acid followed by a normal convulsing dose of the solution of absinth, (0.035 to 0.05 c.c. per pound of animal) did not have any convulsion at all, and five others had only muscular twitchings. If any inference could be drawn from these eleven out of fifteen experiments, it would be that cats in which the blood alkalinity has been reduced by lactic acid, are less susceptible to absinth convulsions than are normal cats. It is well to remember, in this connection, that alkalinity of the blood artificially produced, is a condition entirely different from one in which the reduction has occurred as the result of disturbances or changes in metabolism.

In an additional series of experiments, the animals were given less than a normal "convulsing dose" of absinth, followed by an injection

of the diluted lactic acid. The object of these experiments was to determine whether a convulsion would follow diminution of the blood alkalinity. As shown in the accompanying table, not one of these animals had a convulsion after the diluted lactic acid had been injected and the blood alkalinity thereby reduced. The experiments of this

ABSINTH INJECTIONS AFTER REDUCTION OF BLOOD ALKALINITY

| Cat No. | Weight in Pounds | Amount of Absinth Injected, C.c. | Cubic centimeters per Pound | Result | Cubic centimeters Lactic Acid 1 to 3 Minutes Later | Result |
|---|---|---|---|---|---|---|
| 162 | 6.75 | 0.27 | 0.04 | Convulsion | 6.75 | 0 |
| 163 | 5.25 | 0.18 | 0.035 | Convulsion | 5.25 | 0 |
| 164 | 6.50 | 0.16 | 0.035 | Convulsion | 6.50 | 0 |
| 165 | 5.50 | 0.08 | 0.015 | 0 | 5.50 | 0 |
| 166 | 5.50 | 0.08 | 0.015 | 0 | 5.50 | 0 |
| 167 | 9.00 | 0.18 | 0.02 | 0 | 9.00 | 0 |
| 170 | 4.50 | 0.11 | 0.025 | 0 | 4.50 | 0 |

series show that diminished alkalinity does not favor, nor make an animal more susceptible to, a convulsive attack from absinth but, on the contrary, that diminished alkalinity as such makes the animal rather more resistant. These results suggest that the change in the alkaline reaction of the blood before convulsive attacks in man, found by many investigators, is merely associated with some other factor, and has no etiologic relation to, and does not increase, the susceptibility of the individual to a convulsive attack.

IV. *Animals that have been starved for seventy-two hours are not less susceptible to absinth convulsions than those that have been fed shortly before the injections.*

As has already been mentioned, most of the cats we used did not receive any food for twenty-four hours before the experiments. Of the fourteen cats of series IV, six were fed a few hours before they were used, and eight had been without food for seventy-two hours. The following are a few of the experiments of each group:

| PROCEDURE | RESULT |
|---|---|
| Cat 228. Weight, 6½ pounds. Fed a few hours previously. | |
| 3:54 p. m.: Injection of 0.2 c.c. of absinth in alcohol (0.03 c.c. per pound). | Twitching and rapid breathing. |
| 4:18 p. m.: Injection of 0.26 c.c. (0.04 c.c. per pound). | Convulsion lasting two minutes; twitching. |
| 4:40 p. m.: Injection of 0.26 c.c. | Occasional twitch. |
| Cat 232. Weight, 5½ pounds. Fed a few hours previously. | |
| 3:04 p. m.: Injection of 0.16 c.c. of absinth in alcohol (0.03 c.c. per pound). | No convulsion. |
| 3:47 p. m.: Injection of 0.16 c.c. | One twitch. |

| Procedure | Result |
|---|---|
| 4:17 p. m.: Injection of 0.27 c.c. (0.05 c.c. per pound). | Violent convulsion. |
| 4:40 p. m.: Injection of 0.33 c.c. (0.06 c.c. per pound). | Occasional twitch. |
| Cat 236. Weight, 5 pounds. Fed a few hours previously. | |
| 3:41 p. m.: Injection of 0.17 c.c. of absinth in alcohol (0.035 c.c. per pound). | Violent convulsion. |
| 4:07 p. m.: Injection of 0.2 c.c. (0.04 c.c. per pound). | No convulsion. |
| 4:34 p. m.: Injection of 0.25 c.c. (0.05 c.c. per pound). | No convulsion. |
| Cat 231. Weight, 7½ pounds. No food for seventy-two hours. | |
| 2:59 p. m.: Injection of 0.22 c.c. of absinth in alcohol (0.03 c.c. per pound). | One slight twitch. |
| 3:40 p. m.: Injection of 0.22 c.c. | One twitch. |
| 4:12 p. m.: Injection of 0.37 c.c. (0.05 c.c. per pound). | Violent convulsion with twitches. |
| Cat 235. Weight, 5¾ pounds. No food for seventy-two hours. | |
| 3:27 p. m.: Injection of 0.20 c.c. of absinth in alcohol (0.035 c.c. per pound). | Immediate convulsion. |
| 4:04 p. m.: Injection of 0.23 c.c. (0.04 c.c. per pound). | No convulsion. |
| 4:31 p. m.: Injection of 0.29 c.c. (0.05 c.c. per pound). | No convulsion. |
| Cat 237. Weight, 6¼ pounds. No food for seventy-two hours. | |
| 5:04 p. m.: Injection of 0.19 c.c. of absinth in alcohol (0.03 c.c. per pound). | One twitch. |
| 5:15 p. m.: Injection of 0.31 c.c. (0.05 c.c. per pound). | Very severe convulsion for one minute. |

Especially during the past few years, the claim frequently has been made, and there seems to be considerable clinical evidence to support it, that in so-called epileptics, convulsive attacks occur less frequently if the patients are kept on a low protein diet or are actually starved. In this connection, the results of the experiments of this series give food for thought, for they show that, in animals, the susceptibility to absinth convulsions is not influenced by starvation.

V. *The prevention of the convulsive attacks which follow temporary cerebral anemia by an artificial cerebral circulation during the period of compression of the innominate and subclavian arteries.*

For this series of experiments 107 cats were used. In twenty-six of the animals the nature of the convulsive attacks which follow the cerebral anemia, produced by temporary compression of the innominate and left subclavian arteries, was investigated. In eighty-one cats, an artificial cerebral circulation was established in the following manner: Just before the blood vessels were clamped, a needle was inserted into the left carotid artery and fluid was allowed to run in slowly. The

clamps were then applied to the vessels, and a tape which did not include the trachea, esophagus, carotid arteries or vagus nerves, was tightly tied around the animal's neck. This ligature prevented any of the fluid which was passing through the cerebral blood vessels (excepting a small amount which passed through the veins in the spinal canal and which could not be controlled) from entering the general circulation.

A small opening was quickly made in the right jugular vein so that the injected fluid could escape, or a glass canula was inserted into the vein so that the fluid could be collected and the amount measured. In this way, an artificial cerebral circulation was established. The fluid entered through one carotid artery, circulated through the blood vessels of the brain and escaped through the jugular vein of the opposite side. This artificial circulation was continued during the entire period of the cerebral anemia. The needle in the artery was removed and the canula withdrawn from the jugular vein, just before the clamps were removed from the large arteries of the neck.

a. *Animals in whom normal saline solution or Ringer-Locke solution is allowed to circulate through the vessels of the brain during the period of cerebral anemia, do not have any convulsions after the intracranial circulation is reestablished.*

In order to understand the significance of the above mentioned facts, the reader must remember that convulsions regularly follow the cerebral anemia produced by the temporary clamping of the large vessels of the neck, as described in method B. When, however, this artificial circulation of saline or Ringer-Locke solution is established for the period of the cerebral anemia, convulsions rarely occur. In a few instances, in which the large arteries in the neck were probably unduly traumatized by the clamps, so that clotting occurred, there were slight convulsive seizures, but these cats formed the exception. In the large majority of the experiments, convulsions did not occur, and the animals behaved like normal cats as soon as they had recovered from the ether.

During the period of the cerebral anemia and of the artificial cerebral circulation, most of the animals had to be kept alive by artificial respiration; in some of them respiratory movements returned three to five minutes after the artificial cerebral circulation of saline or Ringer-Locke solution had been established.

This freedom from the convulsions of cerebral anemia, must have been due to one of three conditions: Either the solution injured the motor cells or conducting fibers in the brain, so that no excitatory impulses could be sent out to the muscles, or the saline or Ringer-Locke solution was an efficient substitute for blood for the period

during which it was used; or, finally, the solution used, removed some product of disturbed metabolism which was excitatory for the motor cells. We have not yet been able to determine which of the two last mentioned possibilities is the correct one. It is certain, however, that the saline and Ringer-Locke solutions did not damage and therefore interfere with the excitability of the motor cells. This was proved by the fact that the animals remained susceptible to absinth, so that the injection of a "convulsing dose" of absinth was promptly followed by a typical convulsion.

b. *Hypotonic and hypertonic saline and Ringer-Locke solutions also prevent the convulsive attacks which follow temporary cerebral anemia.*

In these experiments, the salt content of the solutions used for the artificial intracranial circulation was diminished or increased in successive series of animals. Finally, pure distilled water was used at one end and 2 per cent. of salt at the other end of the scale. These variations in the concentration of the solutions used, made no essential difference in the results of the experiments. If the animals survived, they did not have any convulsive attacks. When distilled water was used, hemolysis often occurred and was followed in one-half to one hour by the death of the animal. Two per cent. saline or Ringer-Locke with 2 per cent. of salt usually had a profound effect upon the respiratory center, so that respiratory movements were never reestablished.

## CONCLUSIONS

The experiments described in this paper represent the beginning of our attempt to learn more of the nature of convulsive attacks. Results of experiments must always be applied with some reserve to conditions in the human being, for in man symptoms are a result of a disease process, while in animals symptoms are produced by artificial means. The results of our experiments are, with this reservation, suggestive.

# METABOLIC STATES CONTRIBUTING TO UREMIA*

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The term uremia has been employed in the last few years with two different meanings: to designate a syndrome of symptoms and signs referable to the central nervous system and associated with nephritis; also to designate an increase of the urea in the blood above the normal concentration. In this paper the term will be used in its older sense, namely to designate a state characterized by psychic and motor disorders developing in some cases of nephritis.

Chronic nephritis is a disease of long duration involving not only the kidneys but also the heart, arteries, and possibly other organs. With the number of factors possibly contributing to coma, for example, the problem becomes too complex for direct investigation. On this account uremia developing in cases of acute nephritis offers a better opportunity for study. First the patients are often young and on this account extensive degenerative changes, especially of the heart and arteries are less likely to have occurred. Next the period of duration of the disease is brief, often a matter of days only. And if lesions occur in other organs than the kidneys they are not usually advanced in degree or pronounced in character. The study of cases of acute nephritis and uremia then promises most toward solving the problem of the causation of uremia. Acute nephritis is usually a sequel of some type of infection but often the primary infection has subsided before the first sign of renal disorder appears.

The fact that arrests attention in all types of nephritis is some sort of impairment of excretion. It is this decrease of excretion which measures the degree of severity of the renal disorder, and it matters little in the first instance whether it be water, salt, or some nitrogen compound that fails of excretion. These differences demark types of functional disorder primarily and also, of course, the extent of severity of the lesion.

As a consequence of disordered excretion there results an accumulation of waste products in the organism—retention; when there is retention of water and sodium chlorid, this leads to edema; when of phosphorus, to acidosis in some instances. It was natural to search among waste substances retained in blood and tissues for some one substance which might be held directly responsible for the most striking type of

*Read by invitation, at the third annual meeting of the Association for Research in Nervous and Mental Diseases, New York, Dec. 27, 1922.

uremia, the convulsive type. Some of the known nitrogen compounds excreted in the urine have at some time or other been examined for specific toxicity and tested to determine whether or no, in adequate dosage, any one of them might cause convulsions in animals. The results of experiment have not been decisive. And there is moreover, an insurmountable obstacle to the idea that simple retention of normal waste products can induce uremia. This obstacle is the fact that absolute retention caused either by mercury poisoning, or by the removal of the kidneys in man is not folowed by uremia. Complete anuria resulting from bichlorid of mercury poisoning is not a rare occurrence and we have had opportunity to observe two cases of anuria caused by the removal of the only functioning kidney. There are several such cases reported in the literature. The striking fact is that in cases of this sort there is an enormous accumulation of nitrogen waste products in the body. Determinations of urea and nonprotein nitrogen in the blood give figures higher than those found in the last stage of nephritis, yet these patients develop none of the evidences of uremia. From the experimental side too, comes only negative evidence. Removal of the kidneys in animals, or ligation of the renal vessels or of the ureters produces no characteristic symptom other than the retention shown in chemical analyses of the blood. There is then, no alternative to the conclusion that simple retention is not the immediate cause of uremia, although retention (defective elimination) is the most clear cut consequence of renal disease. There must occur in nephritis a production of some substance foreign to normal catabolism; or the disease nephritis must so change the nervous tissues that they become increasingly sensitive to normal metabolites.

The retention of some chemical compounds at least is not peculiar to nephritis. Thus for example, the retention of sodium chlorid is a conspicuous abnormality in some types of nephritis, but salt retention is notable also in rheumatic fever and pneumonia. There is this difference, however, in the modes of retention in the diseases mentioned. When sodium chlorid is retained in nephritis there is commonly water retention as well and this water retention leads to edema and anasarca. A different state of affairs prevails in the salt retention of febrile diseases. In pneumonia, for example, the sodium chlorid excretion in the urine is only minimal during the febrile period; yet there is no significant water retention during this time. In nephritis, on the other hand, when sodium chlorid is retained there is simultaneous water retention. And the relation of the quantity of salt retained to the amount of water retained seems to be definite and mathematical. This relation is that of the physiologic solution. The experiment of measuring rapid gains in body weight after the ingestion by nephritics with edema of definite amounts of salt has often been made. This gain in

weight is due to retained water and can be predicted often by computation from the salt retention. The retained salt may not be detectable as an excess of chlorids in the plasma, on account of this water retention. Sometimes, however, there is excess of chlorid in blood plasma or blood corpuscles. And the determining factor as to whether the excess of chlorid is in the plasma or the cells seems to be the hydrogen-ion concentration of the blood. Probably this is true for tissue cells as well as blood cells. The probabilities are that the retained chlorid is not in solution, as we ordinarily understand the term, but rather in union with body colloids; as a result, the colloids imbibe more water than normally. We must leave this question here in an unsettled state since our knowledge of colloids is too imperfect to enable us to understand clearly the production of edema. It is not demonstrated as yet for all types of renal disease whether failure of excretion of sodium chlorid is due primarily to inability of the kidney to excrete (as seems the case when plasma chlorid is high) or whether the chlorid is held in a colloidal combination which withholds it from renal filtration. The fact worthy of note is that the retention in renal disease is not a simple retention, but is associated with profound changes in the body chemistry, the cell colloids, and results in water retention and edema.

The subject of edema is fundamental in many problems of neurology. Nephritic edema represents one type and is important in this discussion since edema of the brain is a conspicuous lesion in one kind of uremia. Apropos of the general subject of edema, some basic principles are worthy of note since they have a wide application in disorders of the central nervous system. When the blood supply of a cell is interrupted, a chemical change is at once initiated in that cell. The deprivation of oxygen causes first cellular acidosis and, as a consequence of this reaction, the colloids imbibe water and the cell swells—becomes edematous. This sort of disorder finds examples not only in heart disease, but in circumscribed disease of blood vessels even though the interruption in the circulation is but temporary. One sees then that the same lesion in tissues may be produced in quite different ways. Edema is a colloid change but it may be induced by an excess of salt consequent to renal retention, or it may be induced by cellular asphyxia resulting from a disease in the circulation. This very brief sketch of two contrasting types of edema suggests the reason for similarity in the clinical manifestations between the coma due to nephritic salt retention and the coma of arteriosclerosis.

The second inorganic substance that is sometimes important in uremia is phosphorus. Like chlorid salts the phosphates fail of normal excretion at times and are retained in the tissues. This retention of phosphates leads to acidosis which is sometimes, though rarely, a conspicuous symptom in uremia. The existence of acidosis is demon-

strated by the low hydrogen-ion concentration of the blood and further by therapeutic observation that administration of adequate alkalis relieves alike the symptoms and the signs of acidosis. When it is recalled that the phosphates are the chief agents for maintaining normal reaction in the body fluid it becomes evident how quickly any disorder of phosphate metabolism will declare itself in clinical symptoms.

As explained, none of the nitrogenous waste products found in normal urine can be held directly responsible for convulsive uremia, but the subject of retention of these waste products demands a little further examination. First there is a difference in the facility with which the various known compounds are excreted by the diseased kidney. For example, there may be a definite increase of uric acid in the blood plasma at times when urea and other nitrogenous bodies seem to be normally excreted. This fact has given rise to the idea of selective excretion. A good example of this differentiation of renal function is often noted in chronic nephritis when there is no retention of salt, while at the same time the urea retention is of such a degree that the blood urea is fourfold the normal.

If one determine the amounts of the various nitrogen-containing substances in the urine, e.g., urea, ammonia, uric acid, creatinin, amino-acid, it is found that the sum derived by adding the amounts of nitrogen in these several fractions together just about equals the total nitrogen of the urine. But if we determine the total nonprotein nitrogen in blood, and then the various fractions of which it is composed, the sum of the known fractions does not equal the total. In other words there are nitrogen-containing substances in blood whose character is at present not known, while we know apparently all of the substances in urine. This unknown nitrogen we speak of as the "undetermined" or "rest" nitrogen. Normally the undetermined nitrogen in blood is somewhere about twenty per cent. of the total, but in uremia it is often nearly half. Two possible interpretations suggest themselves in explanation, either the undetermined nitrogen fraction in nephritis finds more difficulty of excretion than any other fraction, or it is produced in excess. Both might conceivably be true. This undetermined nitrogen of blood is doubtless made up of several substances which will eventually be isolated and identified. One of these substances we have thought to be creatinin because of certain reactions, but it is now known that there is no significant amount of creatinin in blood. The behavior of this creatinin-like substance is interesting because in uremic states it increases out of all proportion to other nitrogen waste products. Moreover when there is considerable increase of this *x*-substance, uremia may be predicted.

Since the undetermined nitrogen fraction in urine is very small, in normal blood somewhat larger, and in uremic blood mounts up to thirty or forty per cent., it seems probable that this fraction normally under-

goes transformation into some known waste product; but in severe nephritis and uremia this transformation is slow and imperfect. Where the chemical change occurs and what are the products of this change are not at present known.

Thus far attention has been given to those alterations of the composition of body fluids which result from failure of the kidney as an excretory organ; that is to say to the consequences of retention of waste products. But the kidney is not alone an excretory organ. It is apparently in a sense analytic since it excretes selectively. Whether it is actually synthetic we are not sure. The production of hippuric acid from benzoic acid might be so regarded, but we are not certain that the whole process occurs in the kidney; the liver may be concerned as well.

Ammonia apparently is a product of renal function purely. Formerly we thought of the liver and possibly the muscles as sources of ammonia, but this is no longer the case. If it be recalled that many of the products of normal cell activity are acid in character, and that in various disease states there is an excessive production of acids, then the importance of a source of available alkali in the body can be appreciated. In what degree the failure of ammonia formation contributes to the acidosis of uremic states must be left unanswered. The retention of phosphates already mentioned would conceivably be more rapid in producing clinical effect if combined with a failure of ammonia as a neutralizing agent.

I have endeavored to describe some of the more conspicuous disorders in metabolism which contribute to uremic states. It is the way in which these several disorders are combined that determines the clinical picture and the type of uremia. Retention in nephritis is never pure retention, but is always associated with profound readjustments in the body chemistry. Convulsive uremia, for example, is usually demarked by considerable nitrogen retention, but this is not without exception. In this type of uremia, there seems to be a specific toxic base in the blood; this base has been isolated though never identified. It is conceivable on the basis of analogy that this substance results from a reversal of chemical reaction. In diabetes butyric acid is transformed into hydroxybutyric acid, then into diacetic acid. If for some reason the diacetic acid fails of prompt excretion and accumulates in the body, there results a reversal of the process and the diacetic acid is transformed back into hydroxybutyric acid. So in nephritis a normal process may be reversed by failure of excretion. There are many substances formed in metabolism which are powerful toxins; no effects occur ordinarily because the toxin is promptly transformed into some other substance. But if at the final stage the product were not excreted,

there would at once ensue an increase of all the precursors of these substances, the toxins among them.

All of these various factors with which we have been dealing might be designated as direct factors in the production of uremia, since all of them result from the primary systemic disorder which we call nephritis. Besides these direct factors and most important among them is the state of the circulation. In chronic nephritis, degeneration of the arteries and myocardium is of such frequent occurrence that we often speak of cardiorenal disease, or vascularrenal disease. The vascular hypertension of nephritis is an added strain imposed on a laboring heart so that myocardial insufficiency is a complication of common occurrence. The normal renal function depends primarily on the integrity of the circulation through the kidney. If myocardial weakness induces stasis, renal function is at once impaired. Sometimes cases of nephritis come under observation at a time when the amount of functioning renal tissue seems just sufficient to meet the demands of the individual. The normal latitude to increased demands has gone, conditions are in a state of equilibrium in a restricted environment. Now if there develops myocardial insufficiency with its consequent drop in renal function, uremia develops. In this sense we may quite correctly think of the heart as the immediate agent in precipitating the uremic state.

Nephritis is a constitutional disease, often with pronounced heritable predisposition. The renal lesions and impairments of function are the conspicuous signs; but probably more important are the changes in metabolism which accompany or precede impairment of excretion. Simple retention of excretory substances is the result of lowered renal function; this retention induces profound changes in the body colloids primarily. The delicate adjustment of acid-base equilibrium in the body may be upset by acid retention and by failure of ammonia formation. At times specific toxins are formed, due possibly to a reversal of chemical reactions.

# News and Comment

## THE STATUS OF EPIDEMIC ENCEPHALITIS AS AN INDEPENDENT DISEASE

From the spring of 1920 until recently, there have been comparatively few new cases of epidemic (lethargic) encephalitis in North America, and interest in it has been kept up mainly by the surprising array of its somatic and psychic sequels. Within the last few weeks, however, reports have come of a large epidemic in Winnipeg, and smaller ones in Connecticut and elsewhere. Since 1917, nearly 2,000 articles on this disease have appeared, and, within the last two years, four comprehensive reviews in book form.[1] In addition, the French investigator Levaditi has written a book giving a comparative epidemiologic, pathologic and clinical study of the three closely related acute infectious disorders of the nervous system: encephalitis, poliomyelitis and herpes.[2]

The etiology of both acute encephalitis and poliomyelitis remains unsettled. The champions of the "globoid bodies" of Loewe, Hirschfield and Strauss, and those of the streptococcus, have not yet agreed among themselves, or succeeded in convincing the majority of investigators to accept any exclusive view. It is agreed that the disease is caused by a microbe having a minute filtrable form that permits transmission by means of the filtrable virus to animals. It seems proved also that the virus exists in the nasopharynx, that the disease is mildly contagious, and that the usual period of incubation is ten days. No one now regards seriously the view of the English epidemiologist Crookshank that epidemic encephalitis and poliomyelitis are caused by the same virus or variations of the same virus. The relationship between influenza and encephalitis is most difficult to define. It does not seem reasonable that the appearance of the two diseases in epidemic form at the same time now and in the past can be a mere coincidence. There must be some connection, but what is it? Encephalitis is certainly not a mere sequal of influenza, as most victims of the former do not give a history of having had the latter. Nor do encephalitis patients present the leukopenia and tendency to a peculiar form of pneumonia so characteristic of influenza. Furthermore, there is a form of encephalitis directly connected with influenza, which differs from the epidemic form in being more sudden and severe in its onset, and in having more severe and permanent focal symptoms, more signs of a complicating meningitis, and a marked tendency to multiple minute hemorrhages in the brain and sometimes

1. Acute Epidemic Encephalitis: An Investigation by the Association for Research in Nervous and Mental Disease, New York, 1921. Encephalitis Lethargica, Reports on Public Health and Medical Subjects, No. 11, London 1922. Achard, Charles: L'encéphalite léthargique, Paris, 1921. Sterm, Felix: Die epidemische Encephalitis, Berlin, 1922.

2. Levaditi, C.: Ectodermoses neurotropes: poliomyélite, encéphalite, herpès, Paris, 1922.

to suppuration. Economo has suggested that the encephalitis virus requires activation by that of influenza, and it has also been thought that the damage to vessel walls caused by previous influenza renders a person more susceptible to encephalitis. Another theory, which at least cannot be said to have been positively disproved, is to the effect that encephalitis is caused by a highly neurotropic influenza virus. Stern offers the broad hypothesis that encephalitis is caused by a filtrable virus, which exists in a harmless form in the saliva of many persons, and may be activated not only by the influenza virus, but also by pneumococci, streptococci and other bacteria.

While, as yet, we have no proof of a specific causative virus, the nosologic independence of epidemic encephalitis appears proved when, following Stern, we assemble the main features: First, the clinical ones: (1) the prominence of somnolence, transient cranial nerve palsies, and atonic or hypertonic extrapyramidal motor disturbances (choreic and parkinsonian types); (2) the rarity of certain symptoms that are frequent in other forms of encephalitis, such as those indicative of destructive upper motor neuron lesions, as well as convulsions and anesthesias; (3) the relative frequency of "central" pains, sympathetic disturbances, especially salivation, and certain psuedospontaneous motions and disorders of respiratory rhythm, otherwise more commonly seen in psychogenic disorders than in organic disease; (4) the tendency to frequent variation in the grouping of symptoms in different epidemics and localities; (5) the presence of a chronic progressive form. To these we may add (6) the possibility of the development, after a free interval of years, of a progressive "para-encephalitic disease," analogous to the late nervous manifestations of syphilis. This usually is of a parkinsonian type, and may follow in the wake of an acute illness so mild that its nature becomes established only by the character of the subsequent symptoms.[3]

Anatomically, we have these principal features: (1) the insignificance of the gross changes; (2) the rarity of thrombosis and necrosis; (3) the lymphocytic character of the perivascular infiltrations; (4) the predilection of the inflammation for certain regions of the basal ganglions and brain stem.

Much work has been done on the spinal fluid, and the views, at first quite divergent, have become crystallized. There is no pathognomonic feature, but there are two fluid "syndromes," thus defined by Eskuchen:[4] (1) lymphocytosis; globulin increase; luetic gold curve; increased sugar; (2) cell-globulin "dissociation," with relative increase in cells; luetic gold curve; increased sugar.

On the whole, the most valuable work in the last two years relates to the sequels, mental and physical, the number and variety of groupings of which are most surprising and bewildering, bringing new and unexpected problems in differential diagnosis. Postencephalitic states are easily confused not only with paralysis agitans and chronic choreas, but also with dementia praecox, general paresis, multiple sclerosis and brain tumor. Especially in children, in the absence of history, behavior disorders and other mental disturbances may lead to a wrong diagnosis of imbecility, "moral insanity," or plain unaccountable wickedness.—Editorial, *J. A. M. A.* (March 10) 1923.

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3. This aspect of the encephalitis problem was discussed by Bassoe, Peter: The Diagnosis of Epidemic Encephalitis, J. A. M. A. **79**:2223 (Dec. 30) 1922.

4. Eskuchen, Karl: Ztschr. f. d. ges. Neurol. u. Psychiat. **76**:568, 1922.

## THE TEST OF HYPERTHYROIDISM

The limitations of the so-called Goetsch test as an index of hyperthyroidism have already been pointed out in THE JOURNAL.[1] This reaction consists in the response of patients to subcutaneous injections of small doses of epinephrin, a positive result being manifested by an increase in pulse rate and rise of blood pressure, exaggeration of tremor, palpitation and nervousness, appearing within a short time after the injection. The epinephrin was at first believed to produce sensitization of the organism so that a synergistic action of the thyroid secretion would manifest itself by pressor effects. Although Goetsch originally thought that the phenomenon might be of value in the diagnosis of thyroid disease by allowing a surplus output of thyroid hormone to manifest itself more readily, he later pointed out that the reaction, after all, is indicative only of alterations in the sympathetic system; that is, it becomes an index of sympathetic overstimulation.

In recent studies at the Department of Pharmacology at Columbia University, Lieb and Hyman[2] have demonstrated anew that the reaction to epinephrin measured in the response of blood pressure varies widely with the condition of the subject. This is contrary to the widespread belief that the circulatory system will respond with the accuracy of a chemical balance to any dose of epinephrin.[3] These studies point to the frequency of "variables" in the involuntary nervous system not due to sensitization. They are frequently present when evidences of "tire" are present, and are definitely not associated with hypertonicity of the portion of the nervous system referred to.

Of foremost importance is the observation that the apparent "sensitization" by epinephrin may develop or persist even in the complete absence of thyroid glands. This fact at once indicates that the reaction is due to alterations in the peripheral structures of the involuntary nervous system rather than to changes in the thyroid. The demonstration that the involuntary nervous system is not a "constant" in its responses, and that the variations need not be due to sensitization by some artificially introduced variable such as the thyroid hormone, removes a fundamental postulate of the Goetsch test. It also jeopardizes the validity of the theory which holds that exophthalmic goiter is due to a synergism between the suprarenal medulla and the thyroid gland. As usual, the conflict of opinion is with theories of pathogenesis, not with the facts of direct observation.—*Editorial, J. A. M. A.*, March 24, 1923.

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1. The Goetsch Test in Healthy Persons, editorial, J. A. M. A. **79**:136 (July 8) 1922.

2. Lieb, C. C., and Hyman, H. T.: Studies of Graves' Syndrome and the Involuntary Nervous System, IV, The Vascular Response of the Pithed Cat to Single Intravenous Injections of Adrenalin, Am. J. Physiol. **63**:60 (Dec.,) 1922; V, The Vascular Responses of the Pithed Cat to Repeated Intravenous Injections of Equal Doses of Adrenalin, ibid., p. 68; VI, Attempts to Alter the Vascular Response of the Pithed Cat to Repeated Injections of Similar Doses of Adrenalin, ibid., p. 83; VII, On the Mechanism of Sensitization to Subcutaneous Injections of Adrenalin, ibid., p. 88.

3. Elliott: J. Physiol. **44**:374, 1912.

## CORRECTION

In the article Recent Developments in Electrodiagnosis by Percival Bailey in the April issue of the ARCHIVES on page 441 the equations should read:

$$\frac{a}{b} = RC\left\{\frac{V_o}{V_{rh}} - log_e \frac{V_o}{V_{rh}} - 1\right\}$$

$$\frac{a}{b} = RC\ (2 - log_e 2 - 1) = 0.31\ RC.$$

instead of as printed.

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## AMERICAN NEUROLOGICAL ASSOCIATION

The forty-ninth annual meeting of the American Neurological Association will be held in Boston, May 31, June 1 and 2, 1923.

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## AMERICAN PSYCHIATRIC ASSOCIATION

The annual meeting of the American Psychiatric Association will be held June 19 to 22, 1923, inclusive, at Hotel Statler, Detroit, Mich.

# Abstracts from Current Literature

STUDY OF ANTIPROTEOLYTIC FERMENTS, AMYLASE AND OXYDASE IN FOUR TYPES OF PSYCHOSIS, WITH ESPECIAL CONSIDERATION OF METABOLISM IN MENTAL DISEASE. Yoschiaki Hayaschi, Monatsch. f. Psychiat. u. Neurol. **51**:23 and 94 (Jan. and Feb.) 1922.

The author summarizes the results of his detailed studies: (1) Dementia paralytica: (a) In the acute stage or in an exacerbation of a chronic case the antitryptic content of the spinal fluid is increased. (b) The antitryptic power of the spinal fluid in the chronic stage is very variable; usually there is little or no increase. (c) There is some parallelism between the severity of the case and the antitryptic power of the spinal fluid. (d) The antitryptic power of the spinal fluid is greater in the acute than in the chronic phase. (e) There is some parallelism between the antitryptic power of the serum and that of the spinal fluid. (f) In some cases the amylolytic power of the serum is normal. (g) Remissions of the disease are accompanied by an increase, exacerbations by a decrease, in the amylolytic power of the serum. (h) The amylolytic power of the serum is reduced during the violent outbursts. (i) The amylolytic power of the spinal fluid is very variable; phases of violence and fear are accompanied by a reduction, remissions by an increase. (j) The quantity of oxidative ferments in the serum is generally above normal. (k) The quantity of oxidative ferments in the serum is greater in the violent phases than in the quiet periods. (l) It is probably greater in times of paralytic attacks than in the periods without attacks. (m) The quantity of the oxidative ferment in the spinal fluid is generally increased about 0.64.

(2) Dementia praecox: (a) In the acute phase, or in an exacerbation of a chronic case, there is usually a slight increase in the antitryptic content of the spinal fluid. (b) In chronic stages, the antitryptic power of the spinal fluid is nil. (c) In stuporous states, the antitryptic power of the spinal fluid is very variable. (d) In manic states, the antitryptic power of the spinal fluid is increased more than in stuporous states. (e) The antitryptic power of the spinal fluid is never higher than in progressive paralysis. (f) There is in general a parallelism between the antitryptic power of the serum and the spinal fluid. (g) The amylolytic power is normal. (h) The amylolytic power is never higher than in progressive paralysis. (i) The amylolytic power of the spinal fluid is very variable. (j) Excitement is associated with a decrease, quiet with an increase of the amylolytic power. (k) The oxidative ferments of the serum are generally above the average normal. They are reduced during excited phases, increased during quiet stages. (l) In periods of violence, the oxidative ferments of the serum are greatly increased. (m) In stuporous states the oxidative ferments of the serum are more increased than in the violent phase. (n) The oxidative ferments of the spinal fluid are increased above 0.6.

(3) Mania: (a) The antitryptic power of the serum varies within normal limits; that of the spinal fluid shows no change. (b) In many cases, the amylolytic power of the serum is normal; violent phases are accompanied by diminution, quiet stages with increase. (c) The amylolytic power of the spinal fluid

shows considerable variation. Excitement stages are accompanied by diminution, quiet phases by increase. (d)The oxidative ferments of the serum are below the average, and often below the low normal. (e) Exacerbation is associated with diminution of the oxidative ferment, remission with increase. (f) The oxidative ferment of the spinal fluid is in general below 0.6.

(4) Melancholia: (a) The antitryptic power of the serum varies within normal limits; it shows no variation in the spinal fluid. (b) In melancholia simplex the amylolytic power of the serum is normal. (c) In fear agitation the amylolytic power of the serum is reduced. (d) In fear agitation, the amylolytic power of the spinal fluid is also reduced. (e) The oxidative ferment is below the lower limit of normal. (f) The oxidative ferment content of the serum in fear agitation is above the average normal. (g) The oxidative ferment content of the spinal fluid is generally reduced below 0.6.

(5) Diagnostic notes: (a) It is noteworthy that the antitryptic power of the spinal fluid in dementia paralytica and dementia praecox is increased; in mania and melancholia is within normal limits. (b) There is no relationship between the strength of the amylolytic power of the serum and the type of psychosis, but it is interesting to note that remissions in progressive paralysis are associated with increase in the amylolytic power. (c) Contrary to Kafka's views, there is no connection between the strength of the amylase in the spinal fluid and the type of psychosis. (d) It is noteworthy that the oxidative ferments of the serum are generally above the average normal in dementia paralytica and dementia praecox, and below the average normal in mania and melancholia, with the exception of the fear agitations. (e) It is interesting to note that the oxidative ferments in the spinal fluid is dementia paralytica are over 0.64, in dementia praecox over 0.60, and in mania and melancholia reduced below 0.60. (f) If these data should be confirmed on a larger series of cases, it would be of importance in the differential diagnosis of these conditions.

At the conclusion of an elaborate discussion of metabolism, normal and abnormal, of nucleins, proteids and sugars, he elaborates the following hypotheses for the four psychoses: (1) In dementia paralytica: (a) The disturbance of protein metabolism is not the result of disturbance of the oxidative ferment but of disturbance of the proteolytic ferments and the de-aminizing ferments which hasten hydroclastic reaction and hydrolytic cleavage. (b) The disturbance of nuclein metabolism is the result of disturbance of a true oxidative ferment—xanthoxydase. (c) The disturbance of oxidation of carbohydrates can be explained on the basis of an incomplete action of carboxylase which hastens the Cannizzaro reaction. (2) In dementia praecox: (a) The disturbance of protein metabolism is not caused by disturbance of actual oxidative ferments but by disturbance of proteolytic ferments. (b) The disturbance of nuclein metabolism is caused by disturbance of actual oxidative ferments, more particularly xanthoxydase. (3) In mania: (a) Catabolism and oxidation are increased. The cause of this is unknown. (b) Oxidation processes are disturbed because of lack of oxidative ferments, in spite of increased oxidation, and for this reason run in false tracks. (4) In melancholia simplex: Oxidation processes are not disturbed but catabolism and oxidation are slowed. What causes this is unknown. (5) In involution melancholia: The disturbance in oxidation is not caused by disturbance of the actual oxidative ferment but through a great need for oxygen, or through a disturbance of the fermentative processes which produce the hydroclastic reaction and hasten the related Cannizzaro reaction.

SELLING, Portland, Oregon.

HISTOPATHOLOGIC STUDIES IN PSYCHIATRY. W. SPIELMEYER, Klin. Wchnschr. **1**:1817 (Sept. 9) 1922.

In this article the author reviews some of the fundamental facts in regard to the histopathology of the cortex. He asserts that it is disappointing in a study of such striking conditions as confusional states and epilepsy to find so little of positive value; and if we should review our knowledge of the anatomy of mental diseases, very few conditions could be named in which a definite anatomic lesion could be pointed out. Syphilitic and arteriosclerotic conditions, senile changes, several types of idiocy and a few other isolated conditions make up the entire group about which we have any definite knowledge.

It is not necessary to preach about the hopelessness of anatomic study in psychiatry; the lack of progress in its development is merely a seeming standstill, and one familiar with this field of work cannot be surprised at this when he remembers how little is known about the more commonly recognized cortical conditions. Thus far it is only the gross changes which help us, rarely ever nerve tissue changes. Even in general paralysis and arteriosclerosis the alterations which we study occur in the mesenchyma.

In the large group of degenerative diseases but few histopathologic changes are of diagnostic value. The placques in senile dementia, the ganglion cell changes in Alzheimer's disease and in amaurotic idiocy are outstanding exceptions. Even in dementia praecox in which one would expect to find changes following so much study, investigations up to the present time have been very unsatisfactory.

If one recalls how difficult it is to recognize the ganglion cell changes in the motor groups in such profound conditions as spinal muscular atrophy or bulbar palsy, or to recognize a loss of ganglion cells in idiopathic muscular atrophy, one need not wonder at the difficulty in discovering changes in cells and fibers in the cortex in conditions without disturbance of functional activity. The same difficulty in determining an exact qualitative change is also to be noted in neurologic conditions such as tabes and amyotrophic lateral sclerosis in which the pathologic diagnosis is not based on the character of the nervous tissue change, but on the recurrence of a similar and localized process. Spielmeyer doubts if similar, closely circumscribed, system diseases of the cortex occur. Certainly they are so rare that they have no practical value.

It is interesting that the end results of various processes, as also noted in other organs, resemble one another very closely, and indicates the need of study of the earlier stages of disease. In the past ten years the study of the ganglion cells has again come into its own, and we no longer look for changes in the nerve fibers but study the changes in the nerve cells. To meet this difficult problem, histochemical methods offer a field which is approached with new hope. The study of the neuroglia is of considerable importance. Its reaction is independent of the quality, the grade and the tempo of the disease process. Just how the glia cells dispose of waste products, if they function as phagocytes or if they are affected by the disease process, is of extreme importance, as also the method of protoplasmatic and added changes in the parenchyma.

As Spielmeyer has pointed out in his "Histopathologie des Nervensystems" considerable advance has been made, even though an anatomic reason may not have been determined as yet for isolated disease entities. As the cortical structure is so complicated, attention should be directed to the more simple parts

of the nervous system; the cerebellum has shown changes in chronic processes, as also the Ammon's horn in epilepsy. Anatomic changes should not be considered conclusive until proved by repeated examinations and substantiated clinically.

Alzheimer, with the clinical assistance of Kraepelin, in a most painstaking manner, worked out the histopathology of the disease named after him. The work on amaurotic idiocy has been checked sufficiently to establish a definite picture. The same is true of Wilson's disease and pseudosclerosis. Isolated anatomic findings are of importance, as, with correlation of similar cases, disease groups may be established. This has been demonstrated so well by the diligent and elaborate work of Nissl. Today clinics and well regulated laboratories that work up their material from the clinical and pathologic standpoint can hope to make progress. It is true that pathologic work is chiefly interested in differential diagnosis as in dealing with general paralysis, cerebral syphilis, arteriosclerotic changes and the like. Spielmeyer has seen a case of multiple sclerosis with marked cerebellar changes considered as general paralysis and only correctly diagnosed by microscopic study. The same may be said of Alzheimer's disease and other senile conditions. General paralysis has been taken for dementia praecox and only on section has the error been discovered. Much work of merit has been done on amaurotic idiocy, tuberous sclerosis, and also on traumatic, circulatory, encephalitic, and syphilitic conditions. The study of general paralysis has become more interesting of late due to the work of Jahnel. It is possible that the question of specificity of the spirochete for the nervous system may be answered, as also its reaction on the nervous tissue and blood vessels. Among the encephalitides, general paralysis has the interesting finding that besides the inflammatory changes, there are also associated degenerative changes. Such secondary degenerative changes also occur in spotted fever and epidemic encephalitis. The histologic problems in diagnosing diseases are not settled by indicating the localization of the process and its characteristics. Everybody knows how difficult it is to make a complete and careful histologic study of the brain. The entire problem of histopathology is still in its developmental period and many fundamental facts are as yet unsolved. Thus we know nothing as to why such definite processes as general paralysis and senile dementia affect the Ammon's horn and frontal lobes and why the occipital lobes are left more or less unaffected. The frequency with which the third layer of Brodmann is affected by various diseases also remains a curiosity. We have arrived at no definite conclusion, nor do we know as yet what local pathogenic factors are at work causing some processes to prefer certain cortical zones, and, as Spielmeyer emphasizes, there still remains a great deal of work to be done in the field of histopathology.

MOERSCH, Rochester, Minn.

THE ASSOCIATION BETWEEN TUBERCULOSIS, NEUROPSYCHOPATHY AND DELINQUENCY. ROSOLINO COLELLA, Riv. d. Patol. nerv. e ment. **27**: Oct. 15, 1922.

The problem must have special significance in Sicily where the author is director of the department of nervous diseases in the Universities of Messina and Palermo and also of the Hospital for the Insane of the latter city, which contains about three thousand patients. In his clinic and hospital population, 40 per cent. had tuberculosis, active or latent, and 10 per cent. had syphilis. It was noted by the author alone in 1894, and in conjunction with Frisco in 1914,

that tuberculosis was encountered very frequently in the nervous system. They called attention not only to tuberculous meningitis, tuberculosis of the brain, myelitis, and areas of softening due to thrombosis caused by changes in the vessel walls or to embolism, but also to certain psychic, motor, sensory and trophic disorders. The author also has described tuberculous polyneuritis with or without psychosis. He again describes pathologic and clinical examples of all these conditions, and pays particular attention to the antisocial and delinquent tendencies of those suffering from tuberculosis. The author describes in detail five cases, three of which were subjected to exhaustive anatomic studies. The author investigated spinal nerves, roots and the ganlions of the cord, medulla and pons, the cranial nerves, various portions of the cortex and various muscles. In all cases, necropsies were performed within twenty-four hours. The methods of staining used were those of Orth, Hoyer, Nissl, Weigert and Golgi. He also used methylene blue and hematoxylin. Parenchymatous changes were found in every part of the peripheral nerves, motor, sensory, and mixed, spinal and cranial. These changes were equally as marked in the central nervous system and the spinal roots as in the peripheral nerves. They resulted in either severe motor, with predominant trophic, disturbances or in special painful or anesthetic neuritides. Psychic disturbances were associated with multiple neuritis. Polyneuritis was the first sign in an otherwise latent case of intestinal tuberculosis. Of all the disturbances caused by the tuberculous toxins in the cerebrospinal axis, the mental disturbances presented the most varied picture. These the author differentiates from the polyneuritic psychosis. To the causes of this type of psychosis, namely, influenza, puerperal fever, erysipelas, diabetes, acute rheumatic fever, smallpox, typhoid pneumonia, syphilis, alcohol, lead, arsenic, etc., the author long ago added tuberculosis.

This picture is quite definite and has been described by many authors. But in three of the author's cases there were syndromes of pseudoparesis, manic depressive insanity and dementia. In these cases were found not only degeneration of the peripheral nerves, muscular atrophy, changes in the columns of Goll, vacuolization of the ganglion cells of the anterior horns, softening of the superficial portions of the cortex, but also colloid degeneration of the thyroid. This last finding would point to a toxemia.

The author calls attention especially to the changes in the association fibers of the brain to explain the special characteristics of the polyneuritic psychosis. That the other psychotic symptoms are varied can be seen by the stress laid on various types observed in the experience of many writers. Thus Marie noted the hypochondria, Berenberg the apathy, Ball the unsystematized delirium, Peter the neurasthenia, Boccilli the moral perversions, Clouston the mania of suspicion, etc. The symptoms in the individual case, therefore, vary from simple loss of memory, to impulsive behavior, epileptic seizures with or without psychosis, hallucinations, confusions and occasionally even complete dementia. These symptoms are often preceded by a period of anxiety and great irritability. Occasionally, the first sign of mental trouble is delinquency or immorality. The author makes a great point of his conception that "regardless of the fact that tuberculosis is the causative factor in these cases of nervous and mental disease, the subjects must have a predisposition to neuropathic and psychopathic disturbances." Of his five cases, there was insanity in the mother of the first case, hysteria and alcoholism in that of the second, alcoholism and insanity in the father of the third, etc.

Three of the author's patients committed grave antisocial acts and the author recalls many horrible murders commited in Italy by tuberculous patients. One

killed his sister in the hospital, another his physician, still another the leader of a charitable organization who had assisted him, etc. The author recalls the experiments of Neircoli in which perfectly normal, intelligent, affable patients with tuberculosis became psychically much disturbed after injections of tuberculin.

In the author's experience some of the most common antisocial acts are of a sexual nature. Perhaps even more common than this type of delinquency are the acts against the person. The author thinks that the nucleinic acid contained in the tuberculosis poison, and also the principal component of purin, causes these violent acts by reason of its power to excite function, etc. The crimes against the person committed by the author's patients were committed in a perfectly insane, absurdly brutal, impulsive manner. The author recites in detail, the case of the fifth patient who killed his own wife. In this case the author was able to satisfy the judges that the man was insane, as a result of his tuberculosis. He was committed to a hospital for the insane.

The author also makes a point of the fact that in his experience not only the mental but also the polyneuritic symptoms often improve correspondingly with the improvement in the tuberculosis of the lungs or elsewhere.

In the discussion which followed the reading of the author's paper, it was brought out that in none of the author's work, was he ever able to find the tubercle bacillus, either in the peripheral nerves or in the central nervous system. It was also brought out that he did not feel that there was anything particularly characteristic about the types of mental reaction seen in tuberculosis; perhaps the most frequent reactions were those that resembled paresis, dementia praecox and manic depressive insanity. This, of course, does not take into consideration the typical Korsakow reactions in polyneuritis.

OSNATO, New York.

HYSTERICAL GANGRENE. G. C. BOLTON. Monatsch. f. Psychiat. u. Neurol. **51**:1, 1922.

Numerous vasomotor and trophic disturbances have been described in hysteria: erythema, pemphigus, herpes, purpura, alopecia, premature canities, loss of healthy teeth. There is also hysterical edema, usually associated with hysterical paralysis and contractures, but sometimes independent of them. Charcot described a special form to which he gave the name "Oedème bleu des hystériques." He proved its hysterical origin, in that he could produce it by suggestion under hypnosis, and remove it by suggestion. The type which he described is simply one of many forms of trophoneurotic edema, all variants of a single trophic disturbance. They occur not only in hysterical patients, but also in individuals with neuropathic constitutions. Closely related to them is hysterical gangrene.

Hysterical gangrene has given rise to much disagreement. Some admit its existence, others, with Babinski feel that it is always an artefact (mutilations). Many of the cases are undoubtedly artefacts, many cases of swelling and edema are due to the application of bands, and many of skin necrosis are due to the use of irritants. Careful observation of the patient in bed will allow one to determine definitely whether or not artificial means have been used to produce the lesions. Hysterical gangrene may occur in three forms: (1) Solitary hysterical gangrene. (2) Multiple neurotic gangrene. (3) Herpes gangrenosus hystericus.

Herpes gangrenosus hystericus appears as a herpetic lesion, but differs from ordinary herpes in that it does not conform to a skin nerve or root zone. After the vesicles break, the epidermis desquamates and does not regenerate; in its place appears a superficial patch of gangrene, usually surmounted by a crust. The disease is very obstinate, and resists treatment. If the superficial necroses are artificially produced, they are larger, more irregularly distributed, and heal readily under appropriate treatment.

In multiple neurotic skin gangrene, a number of superficial necroses develop, usually after trauma; the first patch usually appears at the site of the trauma; the interval between the trauma and the onset of gangrene varies from hours to months. The patches are anesthetic; they are often symmetrically placed; in severe cases they may involve almost the entire body. Some cases heal readily, others are very refractory. All these patients are neuropaths, many of them severe hysterics.

Solitary hysterical skin gangrene is much less common than the other types. The gangrenous patch goes deeper and involves all layers of the skin. The author reports a case of this type, in which all chance of artefact was excluded. The patient was 25 years old, unmarried, and very nervous. She belonged rather to the group of constitutional psychopaths than to true hysteria. She was a prostitute and was sent to the hospital to be examined for venereal disease. None was found. While in the hospital she broke a small vase, and in so doing received a slight, superficial wound on the palmar surface of the right hand. A small splinter of glass stuck in the skin; it was easily removed with a forceps. The wound was not infected. This glass splinter worried the patient and she believed that her hand would have to be amputated. Shortly after the injury, there appeared on the back of the hand an area of edema, circumscribed, elastic and rather firm, which the author considers hysterical. The edema disappeared after five days. The zone about the wound on the palm began to show changes on the second day—first anaemic, then brownish, and on the third day, black. This developed into a typical area of gangrene, which included the whole zone of the original wound, and involved skin and subcutaneous tissues. After twelve days the scab began to loosen, and complete healing took place.

In the history of the patient, there are numerous evidences of disturbance in the vegetative nervous system—paraesthesias in hands and feet, dead fingers, feeling of oppression, hyperacidity, dysmenorrhaea, and attacks of urticaria. She also showed such vegetative stigmata as dermatographia, sinus arrhythmia, and oculocardiac reflex.

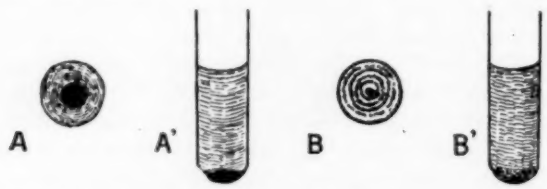
As to the mechanism of production of these lesions, the author offers little. He points out that what one can suggest to a patient in hypnosis, the patient can suggest to himself. And whereas hysterical gangrene has never been definitely produced by hypnotic suggestion, closely allied forms of edema have been so produced and cured. He agrees with Lewandowsky that this entire group of disturbances cannot strictly be classed as hysterical. They occur not only in hysteria, but, as in the above case, in other psychopathic states as well. He believes that a functional vasomotor insufficiency, congenital in origin, is the main factor—a constitutional sympathetic insufficiency, which in turn depends on an insufficiency of those endocrines which keep up the tone of the sympathetic system, especially the thyroid and the chromaffin system.

SELLING, Portland, Oregon.

THE BENZOIN COLLOIDAL REACTION IN 105 NEUROLOGIC CASES. P. Marie, Boultier and Iorgoulesco, Ann. de méd. **12**:263 (Oct.) 1922.

The writers recall that this reaction rests on the mixing of a certain volume of a colloidal suspension of benzoin with an equal volume of cerebrospinal fluid diluted with water in proportions of 3:4, 1:2, 1:4, 1:8, 1:16, 1:32, etc. The phenomenon consists of precipitation of benzoin in the case of specificity. The two ways of doing the test, with five tubes, "reaction simplified," or with sixteen tubes, "reaction complete," have given identical results as regards diagnostic value.

They believe that certain directions are important for the reading of the tests. Often, both in a tube of negative reaction, and in a tube of positive reaction, or, even more, in the case of a subpositive reaction, the mass of the liquid in the tube shows approximately the same clearness. It then becomes necessary to examine the base of the tube. A precipitation due to simple decantation, and indicative of a negative test, can be seen to differ in arrangement from that of a precipitation determined by flocculation (positive). In the negative reactions there is a compact round mass, sharply delimited, situated in the very center of the bottom of the tube. In contrast, in the positive reactions, the bottom of the tube does not present a central pin point mass. Instead there are several concentric rings of precipitate. The diagrams make this clearer.




Precipitate: A and A', base and side of tube in a negative reaction; B and B', base and side of tube in a positive reaction.

Various authors affirm, with reason, that it is possible to read the positivity after 15 minutes and recommend a definite rereading at the end of twelve hours. However, as some positives are late in evolving, the present writers recommend that the second reading be done twenty-four to thirty-six hours after the first. The test proved positive in 33 cases. It was negative in 4 cases of brain tumor, 12 cases of epidemic encephalitis, 1 case of Pott's disease, 6 cases of epilepsy, 2 of psychosis, 1 of senility, and in 56 cases of diverse character, including many functional disorders. The test gave reactions which were parallel with the results of Bordet-Wassermann reactions in all but three cases (two hemiplegias and one Erb's paraplegia), and, in these, later events favored the result obtained with the colloidal benzoin test.

Davis, New York.

THE REACTION OF COLLOIDAL BENZOIN IN GENERAL PARALYSIS. R. Targowla, Presse méd. **30**:931 (Oct. 28) 1922.

The colloidal benzoin reaction of Guillain, Laroche, and Léchelle uses 15 tubes of cerebrospinal fluid in dilutions from 3 in 4 to 1 in 16384. 22222.22222-10000 is the average reaction in general paralysis; "2" indicates total precipitation, "1" and "0", partial and absent precipitation. A "positive reaction" requires

total precipitation in the first five tubes, the "syphilitic zone." Partial precipitation in the first tubes, such as 12220.2222100000, or 11100.2220000000, is rare and indefinite. However, partial precipitation at the end of the "syphilitic zone" is frequently found: 22221. appears almost as diagnostic of general paralysis as does 22222.; and 22200. and 22100. are sometimes found in early cases of the disease.

The writer does not claim that his "positive reaction" is absolutely pathognomonic of general paralysis, but states that every positive benzoin reaction in a series of 400 spinal fluids was verified by typical clinical findings or by necropsy. Six cases in this series were clinically not general paralytics at the time the fluid was first taken, but developed typical symptoms later and thus verified the serologic diagnosis. During clinical remissions, the benzoin reaction remains positive at least to some extent, though less strongly so than during an active phase. Furthermore, the strength of this reaction varies directly with the organic neurologic element causing a period of exacerbation. For example, a strongly positive reaction during an episode of agitation, accompanied or not by an excess of urea content or hypertension of the spinal fluid, points toward an intense and rapidly progressive meningo-encephalitis, against which therapy will be useless; while if the benzoin reaction be only moderately or weakly positive, with excessive urea content and possibly hypertension of the fluid, the agitation is due to a toxic process and should be readily curable. Similarly, a weakly or moderately positive benzoin reaction with normal urea in the fluid during a period of excitement in a general paralytic, favors the diagnosis of a transient manic state.

HUDDLESON, New York.

EXPERIMENTAL OBSERVATIONS ON THE LOCALIZATION OF THE PAIN SENSE IN THE PARIETAL AND DIAPHRAGMATIC PERITONEUM. JOSEPH A. CAPPS and GEORGE H. COLEMAN, Arch. Int. Med. **30**:778 (Dec.) 1922.

The method employed in this study consists essentially of inserting a trocar through a previously anesthetized portion of the abdominal wall and passing silver wires, one beaded and smooth, another relatively sharp, and palpating various areas of the parietal and diaphragmatic peritoneum. In the earlier experiments patients with ascites were chosen; in the later series the abdomen was first inflated with air. It was found that the anterior and lateral portions of the parietal peritoneum, as far as explored, were sensitive to pain from strong pressure of a smooth point or light pressure or lateral movement of a rough point, and that this pain was localized by the patient with considerable accuracy, the error being less than one inch. The localization of pain from stimulation of the diaphragmatic peritoneum was found in no instance to be in the diaphragm but to be referred to some distant point. Stimulation of the outer margin gave rise to pain in the lower costal region and the subcostal abdominal wall; stimulation of the central portion produced pain over a point along the ridge of the trapezius. The authors note that, embryologically, a portion of the diaphragm is derived from cervical myotomes which carry down in their descent portions of the third, fourth, and fifth cervical nerves; these nerves, originally both sensory and motor, fuse to form the phrenic nerve. The sensory function of the phrenic, however, is lost to the extent that while it transmits afferent stimuli, it is unable to register localized sensations in the diaphragm; these are referred along the course of the cutaneous branches of the fourth cervical segment.

VONDERAHE, Philadelphia.

PERUVIAN FOLK LORE. T. Mejía Xesspe. Rev. de Psiquiat. **4**:205 (July) 1922.

In the first instalment of this paper, an attempt is made to analyze certain elements underlying Peruvian habits and beliefs. In the face of modern civilization the natives have retained their inborn melancholy, traditions and superstitions. They are averse to culture, medicine, hygiene and science in general, as they consider these only as masked ways of increasing their needs. As they live from hand to mouth, thrift and prevention are unknown. Life at home turns around its head, the father. Men, women and children spend the day out, the house being only a resting place and warehouse, or rather a "corral" where poultry, rabbits, cattle and humans dwell together. Work is divided among the family; while the father plows, the mother minds the cattle and the children gather wood. This monotonous life never changes except on such occasions as planting and harvesting time, housebuilding, christenings, weddings, burials and holidays. At sowing time, the owner after providing plenty of "chicha" at home, invites all his friends to join. Some mystic rites are indulged in, such as sprinkling the seed with "chicha," singing victory songs, throwing dirt at each other, laying aside the largest grains as amulets, and paying homage to the owners on completion of building. When a child is born, salt and water are placed in his mouth and the devil is warned to keep away. The first haircutting is turned into a celebration. Engagements are made at the age of 10 to 15, and marriages at 15 to 20, the whole matter being arranged by the parents. The best man must make a present of a house, some cattle and a sum of money; his example is followed by parents, relatives and guests. After the wedding dance is over, the newly married couple are locked in together until the best man opens the door during the next day. Sometimes the couple is tied together for a short time with a silver or gold chain or a wool cord as a reminder that they must not separate during life. Adultery is rare, and guilty parties are visited with contempt. Sex ignorance is so deep, that sometimes the bride, after first submitting to the husband's embraces, runs away in horror and even commits suicide. When a corpse is buried, flowers, coca and other herbs are thrown in to keep the dead man from rising, with chicha and water to keep him from burning in hell. After the burial, aromatic herbs and pieces of horn are also placed in as a protection against further deaths. If, on the way to the burial place, the remains seem heavy, the funeral is postponed, as this is considered evidence that the deceased is not yet willing to be buried. Single people and adulterers are buried with downturned faces, symbolizing their unworthiness to see God. In all cases, a few large stones are put on the body to prevent resuscitation.

Moll, Chicago.

SUGAR IN THE BLOOD AND SPINAL FLUID. M. Polonovski and E. Duhot, Presse méd. **31**:60 (Jan. 20) 1923.

This is an analysis of findings obtained by the examination of blood and cerebrospinal fluid taken practically simultaneously, in normal and in pathologic cases. A definite relationship is claimed between the sugar contents of the two fluids in normal individuals. Variations in this ratio are considered more valuable, for the study of pathologic cases, than variations in the spinal fluid sugar content alone. The normal sugar content of spinal fluid appeared to vary over a wider range than is usually believed. It was found to be 0.45 to 0.85 nine to ten hours after a meal, and 0.55 to 1.05 three to five hours after eating.

A reversible reaction seemed to obtain between free sugar and available sugar—explained on the basis of a physical rather than a chemical difference between the two—part of the sugar behaving like a colloid. Glycolysis, breaking down of sugar, was partly counterbalanced by an increase in directly measurable sugar, a "liberation" of sugar. Variable factors like these, hitherto disregarded or inadequately recognized, were deemed responsible for the divergent findings of various authors. Questions of technic as affected by the different colloidal properties of the two mediums (blood and fluid) are discussed in detail.

An equilibrium was noted between the free glucose of whole blood, and that of the spinal fluid, the latter being consistently a little lower. This equilibrium persisted under experimental conditions of hypoglycemia and hyperglycemia, e. g., as influenced by adrenalin; similarly, in diabetes. The increased sugar content of the cerebrospinal fluid commonly encountered in epidemic encephalitis is paralleled by an increase of blood sugar, and is therefore not a purely local phenomenon. In cases of meningitis with diminished spinal fluid sugar, the blood sugar must also be taken; if there is a disproportion between the two findings, its extent will be of diagnostic and prognostic value.

HUDDLESON, New York.

SPINAL ACTINOMYCOSIS. LESNÉ and BELLOIR, Ann. de méd. **12**:329 (Oct.) 1922.

According to Poncet 3 per cent. of cases of actinomycosis show central nervous system localization. In 1911, Arnaudon brought together twenty-seven observations of cerebral localization. In 1919, Sagredo reported two more cases.

Cerebral localization sometimes spreads from a buccopharyngeal lesion. Other times, it is secondary to an abdominal or pulmonary actinomycosis which reaches the brain by the blood stream. "Metastatic actinomycosis most often is due to emboli from the lung, for the lung is very frequently involved." Sometimes the cerebral lesion appears to be primary, with the portal of entry unknown (Enriques and Sicard). The symptoms are those of brain abscess or tumor. A fatal issue in coma is the rule. Occasionally, due to the rupture of an actinomycotic abscess, an acute meningitis ensues and in these instances, lumbar puncture permits one to find the parasite in mycelial tufts in the spinal fluid.

In several cases of vertebral actinomycosis, the spinal cord has been compressed, with resultant paraplegia or quadriplegia. Because the writers do not know of any case in medical literature of actinomycosis with definite location in the spinal cord tissue, they report, with necropsy findings, a case recently encountered. There were dual subcutaneous abscesses, severe and diffuse pulmonary disease with mycelia in the sputum, and in the third month, in spite of treatment, a rapidly established flaccid paraplegia with sphincter disturbance, and in three days total anesthesia in all modes over the legs and up to the level of the umbilicus. The spinal fluid showed only slight albuminosis and 8 lymphocytes per cubic millimeter. The serum of the patient agglutinated cultures of sporotricha and gave the fixation reaction of Widal and Abrami.

Necropsy showed a grouping of very small abscesses in the lower dorsal portion of the cord, each no larger than a millet seed. These were conglomerate inflammatory nodules, almost all of them having typical yellow actinomycotic granules in the center. Near the center of the cord there was dense conjunctivovascular tissue, and more peripherally, and between the small abscess points, intense neurogliar thickening and fibrovascular spaces.

Iodid treatment in actinomycosis is said to be both curative and preventive of emboli. But this form of treatment, while usually so active in cutaneous mycosis, appears to be without any effect in the mycosis of the central nervous system. Finally, in actinomycosis it is well to avoid surgical intervention as much as possible for it can frequently instigate metastasis and generalization.

DAVIS, New York.

OCCIPITAL LOBE EMBOLISM. ANDREW H. WOODS, J. Nerv. & Ment. Dis. **55**:2 (Feb.) 1922.

The first patient, a woman, aged 30 years, developed pain and stiffness in the left side of the neck. After two treatments by an osteopath, right homonymous hemianopia with paresthesia and weakness of the left limbs developed; the latter cleared up within a week. Examination three months later revealed a right homonymous upper quadrantanopia with involvement of one fourth of the macular field. Pressure on the tip of the first and second transverse cervical processes produced pain and increased resistance in the soft tissues of the left suboccipital region, behind the mastoid process. Bending to the right and rotation of the head also caused pain in this region. Laboratory reports and neurologic examination were negative.

The second patient, a man, aged 55 years, was seized suddenly with dizziness, momentary tingling in the left extremities, left homonymous hemianopia, visual paresthesia and disorientation. Two weeks later the visual fields had partly cleared up in the peripheral zone and in thin sectors in both upper and lower quadrants near the vertical meridian. There were no abnormal neurologic findings, but valvular heart disease was present.

The author regards the internal carotids or vertebral arteries as the commonest route of the emboli and states that a backward current through the posterior communicating artery may sweep an embolus from the carotid into the posterior cerebral artery. He found no similar case in the literature. The first embolism is believed to have come from the left vertebral artery and to have been caused by a suppurative process in the surrounding cervical tissues. The immediate mechanism of the tract irritation may have been disturbance of the local blood supply of the cervical cord or merely mechanical.

In the second case the embolus is believed to have affected the sensory tracts in the right thalamic region, and thus to have produced the paresthesia, since this region is supplied by the posterior cerebral artery. From a study of the visual fields, the author believes that the right half of each macula sends fibers only to the right occipital cortex, and the left half only to the left occipital cortex. Partial recovery, such as was seen in the retinal fields in the two cases described, may be due, in the author's opinion, to a slight collateral blood supply, particularly in areas at the periphery, or to a shrinkage of the thrombus. There may have been an initial transitory depression of function in the surrounding areas due to concussion.

STACK, Philadelphia.

THE DIAGNOSIS OF SILENT INTRACRANIAL ABSCESS IN THE AMBULATORY STAGE. HENRI ABOULKER, Presse méd. **30**:474 (June 3) 1922.

The thesis of this paper is that patients with brain abscesses are typically ambulatory up to the precomatose stage; but that the lesions could be dis-

covered and operated on earlier than is now usual. They should be recognized while the patient is still working. The two cardinal symptoms then, as later, are headache and clouding of the intellect with psychic depression. Differentiation must be made from migraine and neurasthenia.

A number of cases are reported, leading to these additional conclusions: (1) that large extradural abscesses, frontal, temporoparietal, or even cerebellar, may remain strictly silent; (2) that the classical symptomatology of encephalic abscess is frequently absent; even in extensive destruction of the temporosphenoidal lobe or of the cerebellum (this symptomatology is ascribed to an increase of pressure in an aseptic cerebrospinal fluid which may develop without an abscess and may or may not occur with one); (3) that local anesthesia should be used at operation, chloroform especially being avoided; (4) that motor disorders are not suggestive of brain abscess, at least not of abscess of otitic origin, since the causes of such cerebral symptoms of a motor character as occurred in the series studied, were found to be quite independent of otitis or abscess.

HUDDLESON, New York.

STUDIES IN ASYMPTOMATIC NEUROSYPHILIS. III. THE APPARENT INFLUENCE OF PREGNANCY ON THE INCIDENCE OF NEUROSYPHILIS IN WOMEN. JOSEPH EARL MOORE, Arch. Int. Med. **30**:548 (Nov.) 1922.

Moore finds in his group of cases that clinical neurosyphilis is three times as frequent in men as in women, although the nervous systems of both, as indicated by spinal fluid findings, are invaded with equal frequency in the early stages. Early syphilis, the author notes, is markedly altered by the simultaneous occurrence of pregnancy, when grave syphilitic lesions tend to be inhibited; spinal fluid abnormalities indicative of syphilis are twice as frequent in a group of sterile women as in a group in which one or more pregnancies have occurred since infection. In consideration of the above data, the author suggests that pregnancy is one factor which may account for the comparative freedom of women from neurosyphilis.

VONDERAHE, Philadelphia.

IS THE STOMACH A FOCUS OF INFECTION? NICHOLAS KOPELOFF, PH.D., Am. J. M. Sc. **165**:120 (Jan.) 1923.

Kopeloff presents a further account and résumé of chemical studies in mental disease and attempts to answer the following question: Has Rehfuss demonstrated that the stomach is a seat of focal infection? Psychiatrists should be highly interested in the report in view of Cotton's claims that: "The stomach and duodenum are very frequently the seat of secondary foci. . . . The bacteria invade the stomach wall and appear to interfere with the secretion of hydrochloric acid, so necessary to digestion. Cultures of the stomach contents will reveal the presence of various types of streptococci and frequently of various types of colon bacilli. The chemical examination of the stomach contents will show either a very low secretion of hydrochloric acid, or, in many cases, its entire absence during the test meal."

The author's chief objections to the method of Rehfuss are: first, that there is little or no value in single determinations; and, second, that he (Rehfuss) neglected consideration of the ingested saliva, and that thereby a tremendous margin of error was produced.

The following observation contains the keynote of Kopeloff's findings: "Bacterial counts showed a striking reduction in numbers in gastric fractions when saliva was inaccessible. The highest number of bacteria per cubic centimeter in a psychotic patient (manic-depressive: manic state) where saliva was *not* removed was 48,000; where saliva *was* removed the highest number found was 32. Similar results were obtained with a normal individual and with other manic patients." The significance of these statements is enhanced when it is recalled that it is a matter of great difficulty to prevent the swallowing of saliva by disturbed and excited patients, and the reduction in the number of bacteria occurred irrespective of the degree of gastric acidity. No normal bacterial flora has been demonstrated; the yeasts, staphylococci, streptococci, and members of the lactic-acid and aerogenes groups which were recovered from the stomach were also found either in the saliva of the same patient or in food which had been given. The conclusions: "The bacteria content of the stomach is influenced by the saliva. The Rehfuss method of fractional gastric analysis cannot be considered an adequate criterion in determining whether the stomach is a focus of infection," seem justifiable and well within the limits of the premises outlined in this article.

STRECKER, Philadelphia.

TREATMENT OF GENERAL PARALYSIS WITH RELAPSING FEVER VIRUS. S. LORENTE Y PATRÓN, Rev. de Psiquiat **4**:193 (July) 1922.

Six male patients with general paralysis were treated with relapsing fever virus, according to Rosenblum's method, and to recent suggestions by Mülhens, Weygandt, Kirschbaum, Plaut and Steiner on the advantages of this procedure. In three subjects, fresh defibrinated blood from a relapsing fever case was used; in one, the inoculation was made directly at the bedside of the relapsing fever case; and in the other two, the blood was taken from the general paralytic who had been inoculated directly, after the presence of the *Spirochaeta recurrentis* has been verified. These last two proved absolutely refractory to the relapsing fever infection, the virus having apparently lost its potency in the transmission. The four successfully inoculated patients (aged 57, 57, 44 and 38 years) improved in varied degrees, especially as regards clinical signs and weight. The cerebrospinal tests, except the colloidal benzoin test, showed little change. Only one 3 c.c. dose of blood was used, except in one case, in which 5 c.c. were injected. Two of the patients had previously been inoculated with malarial blood. The injections were invariably followed by four paroxysms. The patient who presented most clinical improvement was the one who received 5 c.c. of blood, although previous malarial virus injections had yielded no results at all. As these cases were treated between February and May, 1922, and were reported before July, 1922, no definite conclusions can be drawn as to the value of the treatment.

MOLL, Chicago.

ON THE VISCOSITY OF THE CEREBROSPINAL FLUID. T. SODA, J. Nerv. & Ment. Dis. **54**:227 (Sept.) 1921.

The viscosity of the cerebrospinal fluid was determined in twenty-seven cases of disease. In addition, the following constituents of each fluid were determined: protein, total nitrogen, chlorid, inorganic phosphate, alkalinity, and the number of cells. The viscosity showed a tendency to increase with increasing amounts of protein; there was also a parallel between the curves

of alkalinity and viscosity, and between the number of cells and viscosity. The other constituents studied played only a minor part. The author concludes that viscosity determinations of the cerebrospinal fluid are of doubtful value.

VONDERAHE, Philadelphia.

AN UNUSUAL CASE OF MORPHINE POISONING. LEYSER, Monatsch. f. Psychiat. u. Neurol. **51**:12 (Jan.) 1922.

The author reports the case of a morphine addict who developed an acute mental upset (a delirious dream-state), accompanied by certain physical abnormalities: slurring speech; tremulous writing; absent pupillary reflexes; nystagmus; volitional tremor; past pointing; tendency to fall to the left; absent abdominal reflexes. Complete recovery occurred in six days. The differential diagnosis is discussed and the author concludes that the case is one of acute morphine poisoning, although no similar case is on record in the literature. The general picture resembles Wernicke's acute hemorrhagic polioencephalitis. Similar cases due to alcohol, veronal and botulism have been reported. In support of his theory, the author calls attention to the similarity between the action of alcohol (definitely known to produce such syndromes), and morphine.

SELLING, Portland, Oregon.

AN EPIDEMIC OF BOTULISM. C. MOREL and R. DE ST. MARTIN, Presse méd. **30**:829 (Sept. 27) 1922.

One tin of American canned salmon caused symptoms of botulism in 7 of 11 persons who ate small quantities of it. Two of these had only a dryness of the throat with some accompanying difficulty in swallowing; one had, in addition, violent colic and diarrhea. The remaining four exhibited varying degrees of "the classical signs of botulism": asthenia, dryness of the mouth, dysphagia, constipation and the ocular syndrome of paralysis of accommodation, partial amblyopia, choked disk and retraction of the visual fields. Two of the last four cases showed mydriasis, and one a slight unilateral ptosis. All recovered under gastro-intestinal symptomatic treatment and strychnin.

Extended bacteriologic experiments were carried out, and the particular strain of bacillus which was isolated appeared to have low toxin-producing power when compared with that of other strains described in the literature. This was thought to account for the 100 per cent. recovery rate.

HUDDLESON, New York.

BLOOD CREATININ FINDINGS IN FIVE CASES OF CORPUS STRIATUM DISORDER. THEOPHILE RAPHAEL and FREDERICK C. POTTER, J. Nerv. & Ment. Dis. **55**:492 (June) 1922.

The prominence of disturbance of muscle tonus and general motility in disorders of the corpus striatum suggested to the authors the possibility of concomitant alteration in muscle metabolism. The cases studied were two of paralysis agitans, two of Huntington's chorea, and one of congenital double athetosis. Blood urea and urine examinations were made, and the patients were kept in bed on a meat-free diet; on the sixth day blood creatinin was determined. The creatinin content in all instances was definitely below normal.

VONDERAHE, Philadelphia.

# Society Transactions

## THE NEW YORK NEUROLOGICAL SOCIETY

*Regular Meetings, Jan. 2 and Feb. 6, 1923.*

FOSTER KENNEDY, M.D., *President*

### A CASE OF EXTRATHECAL ABSCESS OF THE SPINAL CORD.

DRS. ALFRED S. TAYLOR AND FOSTER KENNEDY.

*History.*—The case here reported was that of a girl aged 15, whose previous history was negative. On November 5, the patient felt a sharp pain over the left lower ribs. Next day the pain continued steadily and she felt chilly. In two more days the pain subsided, but the left lower ribs were sensitive to pressure and a week later a soft swelling appeared at this site. November 17, the legs felt dull and numb and next morning she could not control them and had difficulty in voiding urine. By November 20, there was complete loss of power and sensation in both legs, with loss of sphincter control and slight rigidity of the neck. By lumbar puncture at this time, through the fourth lumbar space, no spinal fluid was obtained, but pure white pus escaped from the needle as it was withdrawn. Her temperature now varied from 101.6 in the morning to 104 in the evening, and she entered the hospital when Dr. Kennedy reported: Motion of the arms and trunk was normal with no stiffness of the neck. The legs seemed to be paralyzed but there was some motion in the flexors of the hip on the right. There was no motion in the toes. On the left the sartorius and vastus internus could be contracted and the toes could be flexed. There was slight rotation of the left ankle. There was complete sphincter palsy. The left abdominal reflexes were absent; the knee jerks and ankle jerks were absent; the plantar reflexes were absent on both sides. There was marked convexity of the outline of the left side over the lower ribs, with tenderness over the five lower ribs. A small tender fluctuating area could be felt over the tenth rib in the anterior axillary line. The left kidney was palpable and tender and there was a large area of dulness to percussion over the left lower ribs, merging with splenic dulness. The lumbar spines were tender to pressure but the spine, as a whole, was not rigid. There was no muscle spasm, so that a primary bony focus in the spine was not present. Sensation was diminished in the first to the fifth sacral areas and this was more notable in the third, fourth and fifth than in the first and second. The lumbar roots were not involved.

Examination of the chest by Dr. Williams showed that the lung was normal except for some compression at the left base. A diagnosis of extrathecal abscess compressing the lower sacral roots was made, the abscess being either metastatic or, more probably, continuous with the subcostal abscess.

*Operation.*—Nov. 21, 1922, Dr. Taylor removed the laminae of the second, third and fourth lumbar vertebrae. Pus was found between the spines of the second and third lumbar vertebrae on the left side as the muscles were separated from the bone. The epidural fat was infiltrated by foci of pus and a white, thick pus escaped when the dura was pushed away from the left side of the spinal canal. The wound was left wide open and freely drained. An

incision was then made over the left tenth rib where the fluctuating swelling was present. A large amount of pus was evacuated when the skin and muscles had been divided. Pus sinuses led between the tenth and eleventh ribs, and on the inner side of the ribs a large, irregular cavity was palpated running downward to the twelfth rib and upward to the eleventh rib. The lower, posterior part of the cavity seemed to lead toward the lumbar spine and probably this was the position from which direct extension to the spinal canal occurred.

*Course.*—From the beginning it was necessary to use a catheter. Cultures of urine on Dec. 4 showed *Bacillus coli communis* and later the urine became turbid. The temperature varied from 99 in the morning to 101.6 in the evening for the first twelve days, and showed slight elevations at times till the thirty-fifth day. Cultures from the pus in the spinal canal and chest revealed *Staphylococcus aureus*, from which a vaccine was prepared. Between November 21 and December 26, blood examination disclosed: hemoglobin, 60 to 75 per cent.; white blood cells, 18,000 (polymorphonuclears, 86 per cent.) to 9,000 (polymorphonuclears, 78 per cent.); red blood cells, 3,500,000.

The wound drained well and filled in rapidly with granulation tissue and finally healed. On the second day the sensory disturbance was much less marked and on this day also the patient began to make some movement in the left thigh and increased motion in the right leg. Sensation improved more rapidly than motor power. On the twenty-seventh day she began to pass urine voluntarily in small amounts at irregular intervals.

Jan. 11, 1923, Dr. Kennedy's examination showed: In the right lower extremity: Flexion at the hip was possible but weak; extension was strong; abduction and adduction of the thigh were both good; neither flexion nor extension was possible at the ankle; no movement of the toes could be performed. In the left leg: extension and flexion of hip present, but weak; flexor and extensor movement was present at the knee; at the ankle, extension and dorsiflexion were present; the toes moved freely; eversion was present, but weak; inversion was present and fairly strong. The right knee jerk was brisk, the left knee jerk obtained; neither ankle jerk was present; the plantar reflexes were absent; abdominal reflexes present; pain and touch sensations were normal in the first sacral areas. Over the third, fourth and fifth sacral root areas there remained only a relative loss of pain and touch sensation. There was no loss of sensation of position in either extremity and deep pain sensation in the calf muscles was increased. She had no knowledge of imminent micturition; she had, however, sensation during the act, but lacked control. The rectal sphincter was paralyzed.

A CASE OF VERTEBRAL DISLOCATION: REDUCTION. Drs. Alfred S. Taylor and Foster Kennedy.

*History.*—The patient, a woman aged 35 years, on Oct. 25, 1922, was thrown from an automobile, landing on her head. She suffered from a small scalp wound on the back of the head, and loss of power and sensation in the trunk and lower extremities. She also suffered great pain, and frequent muscle spasms of the body, legs and neck. Examination by Drs. Pool and Kennedy showed evidences of a transverse lesion at the level of the sixth cervical segment. There was tenderness over the sixth cervical vertebra. Motion was absent in the legs and trunk. In the arms, the biceps and deltoid, both right and left, were intact. The triceps was partially paralyzed on both sides. The hand and forearm muscles were completely paralyzed on both sides. All deep reflexes were abolished. The plantar reflex was absent on the left side and gave slow flexion on the right (not

a normal, but a pathologic sign). Pain (superficial) and touch were abolished to the level of the sixth cervical segment. Loss of appreciation of temperature was at a level about 3 cm. higher than touch or pain. There was a vague sensation of deep pain in the legs and of movements of the toe joints. Roentgenograms taken with a portable machine, showed extreme dislocation forward of the fifth on the sixth cervical vertebra with some crushing of the articular processes on one side. The neck, in the region between the fourth and seventh cervical was extremely tender, both in front and back, but most tender over the fifth and sixth cervical, where there was some deformity, not exactly determinable because of extreme tenderness.

There was a fulness in the front of the neck at the level of sixth cervical vertebra. Breathing was entirely diaphragmatic. Any movement of the head, neck or body caused extreme pain. The temperature on admission was 97, pulse 64, and respiration 20. General health had always been good and she had always been a hard worker. There was a vague story of trouble with the kidneys many years before.

*Operation.*—Oct. 27, 1922, an attempt was made to reduce the dislocation without anesthesia. Stretching of the neck preliminary to the reduction was so painful that a moderate amount of ether was used. After stretching the neck for about five minutes the reduction was accomplished without difficulty. Pictures taken on the spot and developed at once, showed that the alinement, both laterally and anteroposteriorly was practically perfect. The articular processes did not seat entirely home, but were in perfectly good position. She was then put in a plaster jacket involving the whole thorax, shoulders, neck, chin and occiput. From the moment of reduction the pains and muscle spasms disappeared and she could move her head laterally and rotate it slightly in her cast without discomfort. Four days after the reduction another picture was taken in order to make sure of the position. There was perfect alinement, even the articular processes having seated home into their normal positions. She made a slow, but uninterrupted recovery.

*Course.*—The day after admission the temperature reached 99. The day after the reduction of the dislocation (October 27) her temperature reached 101.2 and the next day 101.4; the pulse remained at 82; and respirations, 24 to 28 to the minute. Thereafter her temperature steadily descended and became normal after the eleventh day; her pulse rate averaged from 64 to 78 and her respirations 18 to 24 to the minute. Her urine throughout the period was normal. Her appetite was good and her bowels were kept regular by means of enemas and occasional medication. On the morning after the accident there was slight return of superficial sensation in the legs and thighs that was not present immediately after the accident. The day following the reduction the patient had decidedly more strength in the muscles of the upper extremities, which she had been able to use before reduction had occurred. On the sixth day, following reduction, there occurred definite movement in the toes of the right foot and very slight movement in the great toe of the left foot, although this last was open to question. There was also a faint degree of movement in the thumb of the left hand. On the twenty-second day the patient flexed the third and fourth digits of the right hand. On the twenty-eighth day she moved the second and third digits of the left hand. Movement of the fingers of the right hand is now very much more definite and strong than on the left. There is a slight suspicion of movement in the second and third toes of the left foot. While, at first, breathing was entirely diaphragmatic, within three weeks the intercostals seemed to be working again, although one could not be sure because of the plaster jacket. On the

thirtieth day the patient felt sure that her breathing was almost normal, and one could make out definite excursions of the ribs during respiration. From this time on movement increased steadily. She began to develop the power to raise the left leg off the bed. On the thirty-fifth day, there was very definite increase in strength in the thumb and the first and second fingers of the right hand. On the thirty-eighth day she could move the left big toe very definitely and raise the knee slightly from the bed. On the forty-fifth day another roentgenogram was taken and the spine was found to be still in perfect position. On the forty-ninth day she complained of cramps in the bladder and passed urine spontaneously. On the fiftieth day she voided a large amount of urine voluntarily. From this time on she was able to void more voluntarily (but the pasage of urine was felt only on the left side of the urethra). There was also steady, definite, but slow improvement in all muscles in both the upper and lower extremities. On the fifty-fifth day the cast was split and removed long enough to take an impression for the making of a leather collar and support. Afterward the plaster cast was replaced and held with adhesive plaster.

DISCUSSION

Dr. Foster Kennedy: In regard to the first case, I would like to have Dr. Taylor's opinion regarding the methods of freeing the extrathecal area from pus and granulation tissue. The pressure is slight, but it seems excessively difficult to drain this area and to get sufficient space for adequate drainage.

Dr. Alfred Taylor: The drainage seems to have been satisfactory, and the chances are that the infection has been pretty well overcome. With the inflammatory condition there present, we are bound to have granulation tissue and scar tissue, and we may get pressure later. I believe we should wait several months to see if, in spite of treatment with massage, heat and light, there is permanent cicatrization in the deep tissues, sufficient to cause permanent nerve disturbances. If after that, there is pressure, it would be fair to go into a clean field and try to relieve pressure by secondary operation. As the condition is extradural we have fair hope of success.

Dr. Foster Kennedy: In regard to the second case, a word should be said concerning the method of reduction. Dr. Taylor had a set of ropes from the extension apparatus and braced this round his own hips, so that, with his hand under the girl's neck, and leaning his whole weight backwards, he was able to exert a steady pull until he obtained a perfect reduction of the fracture. The entire procedure took about one hour and ten minutes, a period so long that no steady manual traction could have been maintained

Dr. Charles A. Elsberg: I compliment Dr. Taylor on the way in which he has managed both these cases. My personal experience has been less fortunate with extradural cases. By the time the patient is operated on, he is paraplegic, and after operation, remains so. The cases I have seen have usually been due to acute osteomyelitis of the vertebrae. In the second case the roentgen-ray shows an ideal reduction. There is one point, however, to be noted in these cases of dislocation between the fifth, sixth and seventh cervical vertebrae. One sometimes sees an enormous amount of dislocation in patients who improve and get well. I have seen two such cases—one in a high diver, and one in a football player. Both showed a much more marked dislocation than that indicated by the roentgen-ray in Dr. Taylor's patient. This of course, has no reference to the reduction of the vertebrae obtained in this case by Dr. Taylor which promises ideal results.

DR. I. ABRAHAMSON: Was lumbar puncture done in the second case?

DR. TAYLOR: No.

DR. TAYLOR (Closing): I have seen dislocation with marked deformity persisting in a man who made a perfect neurologic recovery after the accident. Later he was brought to me because of a difficulty in locomotion, due to spasticity in the legs. This occurred after eighteen months. It has been my experience that if angulation persists, in time the upper edge of the lower vertebra causes pressure on the anterior columns and spasticity develops as in the case mentioned.

The technic Dr. Kennedy described, I have used in three different cases. It is original. It suggested itself to me in this case. I did the same thing a number of years ago in a boy who made an almost perfect recovery, except for some slight spasticity in the legs in the morning. It is a simple procedure and well controlled; it gives a very satisfactory anatomic result.

DR. FOSTER KENNEDY (Closing): In regard to the first case, it is difficult to decide whether the extrathecal abscess was a direct extension from the front of the chest, or whether it was a metastatic process. There was evidence of compression of the lower chest, bronchial breathing and dulness to percussion; but apart from that, it was fairly clear that had it been a metastatic, lymphogenous, perineural infection from the lower ribs on the left side, an abscess would have occurred in the mid dorsal region, on account of the obliquity of the intercostal nerves.

## SENSORY DISTURBANCES IN TUMORS OF THE SPINAL CORD AND MEMBANES, AND THEIR DIAGNOSTIC SIGNIFICANCE. DR. CHARLES A. ELSBERG.

The report is based on eighty-seven pathologically verified spinal cord tumors of which fifty-nine were extramedullary, fifteen extradural, and thirteen intramedullary.

Dissociation of cutaneous sensibilities is very frequent in extramedullary tumors, almost as frequent as in intramedullary growths; and in the latter all types of sensation are, frequently, equally involved. The more typical disturbances of sensation in extramedullary, as compared with intramedullary disease are the following: Unless there is a loss of all sensation below the segmental level in many extramedullary growths, the maximum of sensory disturbance is in the most peripheral dermatomes and the minimum of disturbances near the level of the lesion. In intramedullary growths, on the other hand, the maximum of sensory disturbance is often at, and below the segmental level. This difference between the sensory disturbances observed in many intramedullary and extramedullary growths can only be explained on the basis that there is a grouping of fibers in the spinothalamic tracts according to limbs and parts of limbs. Clinical evidence supports the view that in the spinothalamic tracts, the most eccentric and most posterior fibers are those that are distributed to the sacral and lower lumbar dermatomes; that in front and somewhat internal lie the upper lumbar and lower thoracic fibers; still further forward and internal, the upper thoracic, and so on.

The types of sensory disturbances described are more characteristic of extramedullary and intramedullary tumors than the dissociation of sensibility that is ordinarily described. The occasional absence of cutaneous sensory diminution over several dermatomes below the segment level can also be explained on the basis of pressure from behind, which has not yet been transmitted to the most anterior portions of the spinothalamic tracts. Similarly, in tumors on the

anterior aspect of the cord there may be no sensory disturbances in the lower sacral dermatomes and the sensory disturbances therefore are very similar to those seen in intramedullary tumors.

The relative degree of involvement of tactile, pain and temperature sensibility varies considerably. Tactile sensation is rarely more affected than pain and temperature sensibility. Pain and temperature sensibility are sometimes equally diminished, at other times temperature sensibility is more disturbed than pain.

There is often marked dissociation between the ability to recognize hot and cold, and in many cases the patient is unable to recognize hot at a time when he is still able to recognize cold; it is also very interesting that cold may be felt as pain over areas in which pain, as tested with a sharp needle, has been entirely abolished.

There is also frequently a dissociation between vibratory and articular sensibility. Vibratory sensation may be undisturbed while articular sensibilty is profoundly affected or vice versa; or vibratory sensibilty may be profoundly affected on both sides of the body, while articular sensibility is disturbed on only one side.

There are also many variations in the Brown-Séquard picture and in many tumors this type of motor and sensory disturbance is poorly marked. There is generally more motor disturbance on the same side and more sensory change on the opposite side.

In fifteen of the author's series, cutaneous sensation was equally diminished on the two sides of the body, while motor power was more affected on the same side as the tumor, and in five patients both motor power and sensation were most affected on the same side of the body. The author then described the clinical picture which he has called "reverse Brown-Séquard syndrome." He finally stated that in these patients, when bilateral signs become marked, the condition may be one of "bilateral Brown-Séquard" picture.

DISCUSSION

Dr. I. Abrahamson: Dr. Elsberg has approached the subject from a standpoint that is neither stable nor valuable. The stage of the disease when the sensory examinations were made was not mentioned. We all know that late manifestations of tumors of the cord, as well as tumors of the brain, are misleading and that conclusions drawn from them are very hazardous. The better method of approach is the anatomic physiologic method, starting with the first signs of the disease and studying the morbid processes in the order of their development. Variations in sensory changes are not accidental or incidental, but are conditioned by the consistence of the tumor and its position in reference to the level and to the circumference of the cord. The softer tumors, with more widespread root signs, cause tract losses of sensation, earliest and severest just below the level of the disease and diminishing in intensity as they spread downward, often sparing the sacral segments; the hard tumor, with limited root signs, causes the maximum tract sensory disturbances over the lowest sacral distribution with diminishing intensity as we ascend toward the level of the disease.

The position of the tumor with reference to the cord is equally important: lateral pressure causes early and more marked Brown-Séquard syndromes; anterior or posterior pressure causes disturbances of the posterior column sensibility early and intensely and, only later in the disease, irregular disturbances of the pain and temperature sensibility resembling the Brown-Séquard picture.

There are other dissociations between sensory and motor disturbances, and these also depend on the site and degree of the cord compression.

I believe that the signs and symptoms are due, primarily, to circulatory changes within the cord, caused by pressure and interference with the various circulations, and not by the direct pressure on contiguous portions of the cord. I have postulated lamellation of the spinothalamic and other pathways for years; but the type described by Dr. Elsberg, bearing a relationship to the circumference of the cord and not to vascular supply, did not coincide with this view of the matter. The paper of Dr. Elsberg, while interesting, is apt to create confusion in the mind of all but the most expert. The confused sensory charts require proper keys or small diagrams to illustrate the position, age and density of the tumor.

Dr. G. Rosett: How frequently did Dr. Elsberg find sensory and motor disturbance on the same side? In going over the records of a number of cases with Dr. Tilney, I noted a number of cases of lesions of the upper part of the spinal cord in some of which the sensory and motor disturbances were on the same side.

Dr. Friedman: I was glad to hear Dr. Elsberg dispose of the notion that the so-called syringomyelic type of sensory disturbance is found only in intramedullary tumors. We have been making observations similar to those of Dr. Elsberg, with regard to the question of lamellation in the spinothalamic pathways, in the neurologic service of Dr. Kennedy at Bellevue Hospital. We have also found that in extramedullary compression of the cord from side to side, there is the type of sensory change spoken of by Dr. Elsberg. We have termed this a "long tract pressure sign." That the fibers from the lower dermatomes range themselves peripherally in the cord, is also shown by the type of sensory change seen in those tumors of the cord which exert pressure anteroposteriorly. In these cases we get exclusion of the sacral areas with the type of sensory change seen in intramedullary tumors.

I might also suggest that in the few cases in which the motor and sensory signs seem to be on the same side, the mechanism might be that of contrecoup, the motor signs being due to homolateral injury of the pyramidal tract and the sensory changes the result of lesion of the opposite spinothalamic pathway through jamming of the cord against the spinal column.

Dr. Elsberg: When there is a tumor of the anterior aspect of the cord near the median line, one is in doubt whether it is an intramedullary tumor. When the tumors lie mesially on the anterior aspect of the cord, the disturbance is rather of the intramedullary than the extramedullary type.

## SOME REFLECTIONS ON THE MODERN SCHOOL OF DUTCH NEUROPSYCHIATRY. Dr. Smith Ely Jelliffe.

The modern Dutch school of neuropsychiatry probably embraces the greatest number of eminent workers in this field at the present time. The work of the late Dr. J. K. A. Wertheim Salomonson, Rector of the University of Amsterdam, embraced a very wide field, covering a knowledge of medicine, physics, neurology and roentgenology; in the latter branch he was esteemed the chief leader in Holland. He had a lifelong interest in neurology, and devoted considerable time to this subject in later years. His chief researches dealt with the electric degeneration of the peripheral nervous system. Much of his research work was directed toward clinical application, and of this may be mentioned studies on clonus and tetanus, psychogalvanic reflexes, shortening reflexes and measure-

ment of chronaxia. He was also interested in the string galvanometer and applied it to neurological findings.

Prof. C. Winkler, the present Dean of Dutch neuropsychiatry, and director of the University Clinic at Utrecht, is head of a modern psychopathic hospital, and author of a number of works which form a mine of neurologic learning. Winkler early devoted himself to neurology and psychiatry and for many years strove to educate the university in the need to provide special chairs in these subjects. For a long time lack of funds hampered this project and political machinations prevented its fruition, but his idea has now been realized. His life was devoted to the advancement of neuropsychiatry, and he became particularly interested in brain function, at one time making a success as a brain surgeon. During his career Winkler taught many students. He founded the neuropsychiatric society in Amsterdam and became a member of the Royal Academy of Sciences. He founded a Central Institute for Brain Research, of which Ariëns Kappers was made director. At this time also a Central Brain Commission was founded. His work embraced surgical experience, together with anatomic and experimental knowledge, but these were always subordinated to the ideal of therapeutic results. His thought was deep and far-reaching, and his research patient; his therapeutic results were striking. During the early days of the war the University of Utrecht, after many delays, founded a professorship of neuropsychiatry, a goal which Winkler had striven to accomplish for thirty years and Winkler assumed charge of this department. In his works Winkler shows remarkable catholicity of thought, and originality of conception. He is bound by no "school" and is preoccupied by the exploration of that difficult subject, the relation of the "soul" to the body. He is an advocate of the theory that the human body is a capturer, transformer and deliverer of energy.

In considering the enormous field of Winkler's research work, time only permits of the mention of one, perhaps the most interesting. This is his work on the eighth nerve, which he regards as originally a cutaneous nerve and belonging to the oldest group of proprioceptive systems, reaching back in time to the marine habitat. Its functions were first adapted to water shock and later to other forms of pressure. The basis for these studies was work on marine molluscs in which the statocyst organ, influencing the equilibrium of the animal, is the point of departure for a functional study of the labyrinth. Winkler concludes that the labyrinth is the most ancient of sensory organs. He traces the development of vestibular and cochlear nerve components, and the gradual acquisition of sound wave components to the stimuli of aquatic nature. Thus the hearing mechanism has evolved out of the primitive water shock mechanism of the statocyst to respond more and more to air shock reflex activities. A further development of cochlear responses is along the line of audition, rhythmic movement reflexes (dancing, singing) and finally speech activities. Thus hearing and speech conserve, as a heritage of ancient function, the power of reproducing by reflex pathways the phenomena which have given place to the stimulus.

Another important phase of the work by the Dutch school, is that on muscle tonus, in connection with which must be mentioned the names of deBoer, Boeke, Dusser, deBarenne, van Rijnberk, Winkler, Jelgersma, Magnus and Kleijn, and Brouwer.

There has been considerable research, and also difference of opinion among Dutch workers, regarding the so-called double innervation of striped muscle tissue. Boeke established the existence of small neurofibrillar end rings, and end nets, at the end of fine non-medullated nerve fibers, differing entirely from

ordinary end plates. While the morphology is fairly well established, the physiology of these plates is still under active discussion. Plastic mechanical factors, as opposed to the view of chemical nutritive factors, are the main contentions. Pekelharing has mainly studied the latter viewpoint, while deBoer has been one of the most active in claiming the existence of plastic tonus function. DeBoer, experimenting along the lines of pharmacodynamics concludes that skeletal muscle tonus has a definite peripheral autonomic reflex arc component. Numerous correllates would be the outgrowth of such a conception, embracing many experimental and clinical possibilities.

Passing on to the work of von Rijnberk on muscle tonus, the theory of this worker was that there was a vegetative supply to striped muscle, and this was utilized to account for Vulpian's lingual paradox. This theory may help to explain the muscular tonic phenomena following facial palsies, and explain the "foot phenomena" of Sherrington.

Certain phases of the same problem have been extensively studied by Magnus and Kleijn, of the department of pharmacology of the University of Utrecht. They have concerned themselves with the study of decerebrate rigidity and find that the cerebellum plays no part in this syndrome. These workers have separated the labyrinthine from the neck reflexes; the former arise from stimulation of the otoliths, the latter from proprioceptive nerve endings of the cervical muscles. Kleijn describes four components in the postural reflex: (1) head labyrinthine reflex; (2) body wall reflexes influencing head positions; (3) neck muscle reflexes; and (4) trunk and limb muscle reflexes.

Prominent among the workers on cerebellar physiology and morphology are Elliot Smith and Bolk, both of whom are innovators and originators of a new concept. The comparative anatomy of lower species is studied, working from below upward in the scale of organisms, and the conclusion is reached that the several parts recognizable in the mammalian cerebellum have definite functional significance and represent areas of central control over definite motor performances in the body. Bolk has mapped out the various divisions and subdivisions of the cerebellum and finds striking variations between different organs. He believes there is functional variation related to structural variation, since the form is dependent on function. He traces the relationship of various parts of the cerebellar cortex to the body movements (bilateral synergic, or unilateral synergic) with which they are associated. The work of Bolk, preeminently anatomic, has been confirmed by other workers, through animal experimentation.

Jelgersma, professor of psychiatry in the University of Leyden, studied paralysis agitans and has demonstrated alterations of the striated fiber system. His studies on the cerebellum have shown that only two feeling qualities are localizable in this organ, namely: deep sensibility of muscle and joint; and secondly, tonus and equilibrium. Time will show whether these views are correct. Jelgersma has written a masterly text-book on psychiatry. Like many of the younger Dutch neuropsychiatrists, he is greatly interested in psychanalysis.

Ariëns Kappers is director of the Central Institute for Brain Research, and a pupil of Winkler. He has done considerable work on the comparative anatomy of the nervous system. His thought is along the line of conception of organizing synthetic function of the nervous system in response to cosmic stimuli, and he holds that a structural evolution is going on within the nervous system, which he terms neurobiotaxis. He believes function is primary; structure is secondary and variable according to the needs of the organism.

Dr. Jelliffe then took up the work of several other members of the Dutch school and gave illustrations from their works, particularly B. Brouwer, H.

and G. C. Bolten, and L. and H. Boumann. Among other things Dr. Jelliffe pointed out the contributions of Brouwer to the study of the cerebellum and the olives, and drew particular attention to his work on the oculomotor nuclei. Brouwer's utilization of the evolutionary history of neurologic structures makes his work particularly valuable. His study of multiple sclerosis from a phyletic viewpoint was mentioned and illustrated.

Dr. Jelliffe then called attention to the work on the sympathetic nervous system by the Boltens which lay close to his (Dr. Jelliffe's) interests, and then gave a very short sketch of the psychiatric opportunities in Amsterdam with the two psychiatric clinics.

DISCUSSION

Dr. Walter M. Kraus: Dr. Jelliffe, in his delightful review of the work of the Dutch school, has focussed our attention on subjects with which we ordinarily would not have come in contact. He has reviewed a number of interesting neurologic topics of great value. I suppose that research activities in neurology could be divided into three parts: In one, the subject is approached from the viewpoint of formal psychology and, with practically no organic basis, an attempt is made to unravel the most complicated reactions of the human brain. Another group devotes itself to the study of facts as they occur, without being much concerned with their significance in terms of past or future evolution. The third group is interested in tracing the evolution of the human nervous system. As Dr. Jelliffe has emphasized, this last method is essential to the solution of most problems in neurology.

While in Amsterdam, I had a short interview with Dr. Kappers, which was very stimulating. His collection of comparative anatomic material is the finest in the world, and the opportunities for research, which this vast collection offers, would keep a score of men busy for a long time. For those who find it impossible to go and work with Dr. Kappers, his textbook on comparative neurology and his papers on this subject will constitute a source of much information and inspiration to work.

To mention a few things which may be found in his book to stimulate interest in the phylogenetic significance of certain parts of the nervous system: The pyramidal tract, which we have dignified with so many functions, is present only in mammals. Bearing this in mind and also recalling that the pyramidal tract forces its way through the striatum, we derive some notion of a reason for the frequency of hemorrhage from the blood supply of the pyramidal system in the capsular region. Obviously, these blood vessels must be comparatively recent from a phylogenetic point of view and may be expected to be more easily irritated by toxins and thus more easily diseased. In another place Kappers states that in the lower mammals the pyramidal tract appears in the posterior column. Other fibers in these latter columns convey sensation through several relays to the cortex. One wonders, in the light of Kappers' theory of neurobiotaxis, why the pyramidal tract wandered from this position to its present position in the lateral columns.

The nucleus of the twelfth nerve in lower animals without a tongue lies on the ventral side of the medulla. After the tongue appeared, the nucleus assumed a dorsal position in contiguity with the sensory nuclei concerned with the various sensations received from the tongue. This is a beautiful example of neurobiotactic activity. In order to understand the functions of the nervous system as they appear in man it is essential to study their phylogenetic history.

## PHILADELPHIA NEUROLOGICAL SOCIETY

*Regular Meeting, Feb. 23, 1923*

DR. C. M. BYRNES, *President*

### A CASE WITH UNUSUAL MENTAL SYMPTOMS. DR. E. V. EYMAN.

*History.*—A married man, aged 29, was admitted April 17, 1922, to the Pennsylvania Hospital for Mental and Nervous Diseases. His family history was negative. He had a small depression in the left parietal region near the vertex caused by a stone at 8 years of age. He had acute rheumatic fever in October, 1917, while in the navy and has never felt well since. He suffered a fracture of the left arm and a laceration of the scalp over the old depression in November, 1917. Severe headache started after he received the injuries recited and persisted constantly till Feb. 9, 1923. One month after the onset his memory became poor, but he performed his duties on the ship till discharged in February, 1919. At that time he was irritable, restless, had diplopia occasionally, and fell asleep readily. He attempted to resume his duties as an electrician, but his poor memory and absent-mindedness caused him to receive several severe shocks. He then became a masseur. The headache continued and his memory grew worse. He had difficulty in finding his way home, sometimes wandering for hours, but eventually reaching his destination. He became sullen, suspicious, showed increased sexual excitability, developed ideas of marital infidelity and said he had "imaginations."

*Physical Examination.*—The general examination was negative except for the usual signs of aortic regurgitation. When tested for Romberg's sign he always started to fall and then staggered backward and to the right; when walking blind-folded, he turned to the right in a large arc. He responded to commands very slowly. Spontaneous movements were often quickly performed if associated with every-day acts. The face was expressionless and mask-like. The cranial nerves, including the olfactory nerves, were normal with the exception that both retinas were moderately congested, with slight blurring of the nasal disk margins. The neurologic examination otherwise was negative.

*Laboratory Findings.*—Examination of the urine showed albumen, hyaline and granular casts. The Wassermann test and spinal fluid were negative. The roentgenogram of the skull was also negative.

*Mental Examination.*—Memory for recent and remote events was almost nil. He was not depressed, but extreme retardation in cerebration was present; it took him ten minutes to say that a nickel was money, fifteen minutes more to say it was 5 cents, and five minutes to say it was used to buy things. It took him forty-five minutes to find his way back to his ward. He did not recognize his wife or child, but in spite of all this he could play a good game of checkers, pool or baseball, and find his way to the toilet. He occasionally experienced difficulty in finding his room. His mental condition resembled none of the psychoses.

*Course.*—During his hospital residence the patient's memory grew gradually worse, as did his retardation, until February 9, when he suddenly cleared up. For a time after his sudden recovery, his memory for the past six years consisted merely of a few hazy patches, but he has gradually improved in this respect until his memory seems good for everything except the period of his

hospitalization from April, 1922, to February, 1923. His memory for dates for the years immediately following his discharge is still somewhat uncertain. He was seen by many physicians during his illness and a list of some of the diagnoses then made follows: (1) traumatic psychosis; (2) frontal lobe tumor; (3) post-encephalitic condition; (4) manic-depressive depression; and (5) hysteria.

In favor of frontal lobe tumor were the constant headaches, great memory defect, difficulty in finding his way home, and the gradual progression of the condition. Against it were the integrity of olfactory sense and absence of positive changes in the fundus. Tumor is of course ruled out by the patient's recovery. In favor of a post-encephalitic condition was the history of diplopia, drowsiness, the mask-like face, and the slowness of movement in response to command. The suddenness of the recovery seems incompatible with this diagnosis. In favor of the diagnosis of traumatic psychosis we have a fairly definite history of onset following severe injury, but the slowness with which the patient's condition reached its peak does not seem compatible with this diagnosis. Favoring hysteria are the absence of definite neurologic findings, some inconsistencies in the mental symptoms, and the sudden recovery; but again the gradual onset, and the very prolonged duration of a monotonously colorless picture seem unusual. In favor of manic-depressive depression, is the presence of retardation; but the retardation did not include habitual acts such as eating, and there was no very marked depression. My own diagnosis previous to the recovery was a post-encephalitic condition; now it is hysteria.

DISCUSSION

Dr. Alfred J. Ostheimer: This man is a naval ex-service man and I have had him under observation for over a year. I shall add a few points to the history given by Dr. Eyman. The man has a marked depression of the skull, but the navy records show that he had this depression when he first enlisted thirteen years ago. I conclude, therefore, that the old fracture of the skull has had nothing to do with his present condition. There is no doubt that he had a severe accident during recent service, but I think it was not an etiologic factor in his recent mental condition. He had an attack that was called influenza in 1918, and, early in 1919, developed these mental symptoms, with irritability and complete change of character. This man had a very good record in the navy. After he came home he was unable to retain his position as electrician because of irritability, dulness, lethargy and lack of ability to concentrate on his work. Dr. Eyman says that one of the facts that is not compatible with a diagnosis of a post-encephalitic psychosis is that his mental condition has cleared up so quickly. He did not clear up over night. The whole description, I think, corresponds to the rather bizzare character of a post-encephalitic psychosis, notwithstanding the fact that he has recovered rather promptly. I am inclined to believe that the man has had a post-encephalitic psychosis, a long time after the acute attack to be sure, but comparable organically to the parkinsonian syndrome seen so frequently now and manifesting itself one, two or even three years after the acute infectious disease, probably consequent on degenerative structure changes. It may be that I am somewhat influenced by the present policy in the U. S. Veterans' Bureau of giving the man the benefit of the doubt in order to be sure to give him justice, and therefore compensation for a service-connected disability. In this case it seems to me that there is a question of doubt, and when there is a question of doubt, it should be resolved in favor of the man.

## HEMICHOREA OF SUDDEN ONSET IN WHICH THERE WERE NO OTHER SYMPTOMS. S. F. GILPIN, M.D.

The following case is presented because, in the six months that the patient was under observation, there were present only choreo-athetoid movements in the left arm and leg, although in the beginning the movements were also present in the left side of the face. Repeated examinations demonstrated no other symptoms. Such a case is most unusual and difficult to localize. It illustrates, however, that limited lesions may produce athetoid movements only.

*History.*—A white woman, American by birth, 57 years of age, a widow with one son who is in good health, has a negative family history. She was in the Jefferson Hospital twelve years ago for some inflammatory condition of both knees and was operated on in the University Hospital six years ago, an ovarian cyst and the right ovary being removed. For several months she has been troubled with frequent micturition and swelling of the ankles. The present illness began suddenly Aug. 31, 1922. While going from one room to another she felt dizzy and swayed against the stair-rail. Immediately afterward she walked two blocks to my office, and then presented the choreiform movements as seen at present.

*Physical Examination.*—The patient shows no motor weakness, sensation is normal and the pupils, reflexes and laboratory examinations are negative.

## ERB'S TYPE OF SPINAL SYPHILIS PRESENTING DIFFICULTIES IN DIAGNOSIS. S. F. GILPIN, M.D.

The patient, a white woman, aged 52, was admitted to the hospital from the dispensary Dec. 15, 1922. In spite of a negative Wassermann test she had been considered syphilitic and was given mercury by inunction; but by mistake she used double the amount of mercury ordered. In four days she came to the clinic with such severe salivation that she was admitted to the ward for treatment. Her chief complaint was pain beneath the shoulders, in the groins, the balls of the feet, the heels and pain of shooting character in the backs of the legs. She is married but has never been pregnant and has been an actress. She has always had good health, except for the present trouble which began five years ago and has become much worse during the past six months. For the past four months she has been unable to walk in the dark for fear of falling.

Physical examination reveals ataxy of gait and station. The pupils are equal but react sluggishly to light. The knee-jerks are increased, but there is no clonus nor Babinski sign. Repeated examinations of the blood and spinal fluid have yielded negative Wassermann tests; four cells were reported in the spinal fluid at one examination. A second laboratory reported a doubtful (+) Wasserman reaction in the spinal fluid. Roentgen ray examination of the dorsal and lumbar spine was negative. She rapidly became worse, her legs became so weak that she could not get out of bed and she developed marked distention of the abdomen, although surgical and gynecologic examinations proved negative. The distended abdomen was thought to be due to gas, secondary to relaxed or paralyzed intestinal muscle. Believing the case to be syphilitic in spite of the negative Wassermann reactions, she was subjected to the therapeutic test of rapidly increasing doses of iodids. She tolerated the treatment well and rapidly improved. At present she is taking 100 grains (6.3 gm.) of sodium iodid three times daily; she has no pain, can stand and walk without ataxia and her knee-jerks are normal. Did this patient have syphilis? If so why was the Wassermann test persistently negative except for

a + reaction on one occasion? If she does not have syphilis, why did she improve so marvelously under iodids? Is the old fashioned therapeutic test more reliable in the diagnosis of a difficult case of syphilis than the Wassermann test?

DISCUSSION

DR. CHARLES K. MILLS: Regarding Dr. Gilpin's first case, he reported no loss of sensation on either the hemichoreic or the other side. The case is a difficult one for diagnosis. At first sight, I thought it might be an instance of a lesion of the superior cerebellar peduncle, but in the absence of impairment of sensation, it is not possible to explain the case in this way. The only explanation I can see is that there is a focal lesion in some part of the striate body.

DR. FRANCIS X. DERCUM: My own feeling was that, in this case of hemichorea, there was a limited lesion of the striate body and that the movements were in a sense comparable to those which we occasionally see in encephalitis. Several years ago I described two cases of hemichorea of rather rapid onset.

The second case of Dr. Gilpin is interesting because the woman had a pronounced paraplegia. I regarded the case as one of Erb's form of spinal syphilis. The laboratory reports came in repeatedly negative, but in view of the very clear clinical findings I set these reports aside. My attitude in general, in regard to the Wassermann reports, is to assign to them a secondary importance, especially when the clinical findings are positive. This case is remarkable because of the brilliant results following the administration of the iodids in massive doses. This woman was almost completely paraplegic, she stumbled and fell when she attempted to walk but at the present time she walks with a normal gait. We have fallen in a measure under the spell of arsphenamin administration and frequently neglect the massive administration of the iodids. Here is an instance of a result not infrequent among the older neurologists, a brilliant recovery from the use of large doses of the iodids, especially when it is employed in early cases.

DR. W. G. SPILLER: It is interesting to note that S. A. Kinnier Wilson, in a paper recently published, states that the best treatment for syphilis of the nervous sysem would be the intradural injection of mercury if we had a form of mercury that was not irritant. Negative Wassermann findings do not always exclude syphilis, and we do not always obtain positive findings in tabes, which is a syphilitic disease.

DR. S. F. GILPIN: As to the treatment of the second case, I hope that the time will come when the medical profession will realize that, in the treatment of neurosyphilis, it is not necessary to inject anything into the subarachnoid space to get results. It is now four years since I showed a case of tabes to this society, in which the Wassermann reaction and cell count became negative. The patient's gait and station became normal, although she had been so ataxic that she required assistance to come to the clinic. The disease had existed four years before she came under treatment. She has not received treatment for five years and the Wassermann reaction and cells remain negative. The patient had mercury, by inunction only, with systematic drainage of the cerebrospinal fluid. The results in her case have been duplicated in others.

## ILLUMINATING GAS POISONING: REPORT OF A CASE PRESENTING AN UNUSUAL SEQUELA. GEORGE WILSON, M.D.

*History.*—F. S., a white man, aged 60, was admitted to the Episcopal Hospital on Dec. 25, 1922, in an unconscious condition. The night before he was

visiting in a strange house and is clear about events until 10:30 that evening, when he became unconscious and remained so until late the following afternoon. According to the history brought by the police, he was found in a gas-filled room. When he regained consciousness, he complained of pain in the right hip and showed evidences of bruises on the left knee and right temple, these being apparently of small moment. Four days after the occurrence recited he awoke from a sound sleep and found that he could not move the right foot, although he could move the knee, and that the entire lower extremity was greatly swollen. At no time has he had any pain except a pain in the right hip, which was first noticed when he regained consciousness. He has had no headache, no diplopia, and no disturbance of the sphincters.

*Physical Examination.*—Jan. 9, 1923: Pupils, cranial nerves, both upper and the left lower extremities are normal. The abdominal reflexes are absent, probably because of obesity. The entire right lower extremity is much swollen, the swelling being due to edema that pits on pressure. All movements of the right foot are lost, but movements of the right knee and hip are well performed. The right lower extremity lies in a position of helpless eversion, a position frequently assumed in fracture of the hip. The sense of position is severely disturbed in the toes of the right foot. Touch, pain, heat and cold sensibilities are lost in the right extremity as high as the lower third of the leg; from that point to the knee there is diminution of these forms of sensation, which are normal in the thigh. No disturbance of sensation is present in the left lower extremity. Both patellar reflexes are present and active; the Achilles reflex is present on the left and absent on the right. Plantar stimulation produces flexion on the left and no response on the right. Electrical reactions on Feb. 20, 1923, showed feeble reaction to faradism in the affected muscles. Dr. Fewell reported no changes in the optic nerves. Dr. Bromer made the following roentgen-ray report: There is slight roughening of the articular borders of the head of the right femur and of the acetabulum; marked bone proliferation and roughening of the joint surfaces of the tenth, eleventh and twelfth dorsal, and of the first and second lumbar vertebrae are present.

On the day of admission to the hospital, the red cells numbered 6,400,000; white cells, 22,000; and hemoglobin, 95 per cent. Four days later his white cells had dropped to 14,160 and two weeks later were normal. Examination of the urine on two occasions showed the presence of albumen and casts. The blod Wasserman reaction on December 29, was negative.

The localization of the lesion in this case seems to be in the cord in the epiconal region on the right side. This would explain the paralysis and the loss of sensation. The edema was probably due to vasomotor paralysis.

### DISCUSSION

Dr. William G. Spiller: I do not think Dr. Wilson has sufficiently excluded the possibility of vascular thrombosis in this case. He and I have been interested in phlebitis of the upper limb, and phlebitis of the lower limb is well recognized. In some cases the thrombus forms in an artery. The symptoms probably are not produced by pressure of the thrombotic vessel, but by impairment of the circulation to the peripheral nerves.

Dr. George Wilson: This case does not impress me as one of disease of either the femoral artery or femoral vein. It obviously is not a disease of the artery because of the edema. The single fact that the man did not have pain rules out the possibility of phlebitis.

## MOTHER AND DAUGHTER PRESENTING SYMPTOMS OF A DEGENERATIVE STATE OF THE CENTRAL NERVOUS SYSTEM.

ALFRED GORDON, M.D.

The mother aged 56, was in good health until seventeen years ago, when she first observed an awkwardness in the fingers of one hand which was followed by a gradual wasting of the muscles of the hands. The atrophy slowly involved the lower extremities and finally the muscles of the thorax and of the face. When first examined about ten years ago she presented, with one exception, the same condition she now shows. The exception consists in the state of the patellar tendon reflexes which were then increased, but are now abolished.

At present the picture is that of progressive muscular atrophy of the spinal type. The tongue presents a fine tremor; it also is somewhat flabby, but its power is still preserved. The jaw reflex is present and slightly increased. Sensation is normal all over the body and the sphincters are intact. The eye examination shows a convergent right eye; the pupils are 2.5 mm., the right slightly irregular, and both react sluggishly to light and accommodation. The retinal veins are somewhat tortuous, otherwise the eyegrounds are negative. She has a steppage gait. There is slight incoordination in walking, very likely because of the atrophic condition of the extensor muscles. Lately she has developed some difficulty of deglutition and of respiration.

During her entire illness she has not suffered from pain. The blood Wassermann reaction is negative. She has had four children, three of whom died at an early age.

The living child is a girl of 16, who has always had good general health, but noticed difficulty in walking several months ago. Physical examination reveals: a slight Romberg sign; the gait is somewhat difficult, because of the equinus position of the feet which are short, the toes being claw-like because of forced extension. The patellar and Achilles' reflexes are lost. A Babinski sign is present, more frequently on the right than on the left side. In every other respect the patient is normal. The case evidently belongs to the category of Friedreich's ataxia. The characteristic feet, the slight ataxia of station, the absence of tendon reflexes, the presence of the toe-phenomenon, the onset of the disorder at the age of puberty—all speak in favor of the above diagnosis, although there is no nystagmus, involvement of speech, nor ataxia of the upper extremities. It may be of interest to note that the appearance of the disorder dates from the time she commenced to use her lower extremities to excess, being obliged by her occupation to stand almost the entire day. This is in conformity with Edinger's "Ersatz-Theorie"—the theory of exhaustion, which explains the onset of the symptoms of Friedreich's ataxia at the age of puberty.

The occurrence of the two cases in the same family demonstrates a lack of development or of resistance of the central nervous system—in the mother of the ganglion cells and in the daughter of the tracts of white matter.

## FOUR CASES OF POST-ENCEPHALITIC SEQUELAE.

A. M. ORNSTEEN, M.D.

CASE 1.—A married woman, aged 26, in 1918 had influenza, during which she was drowsy. Two years later, during pregnancy, she was markedly lethargic in spells, falling asleep in the midst of the most interesting environments. This continued for six months, the lethargy being attributed to the kidney toxemia

of pregnancy. On the delivery table, the right leg began to tremble and has not stopped since. From that time there has been a steady progression of the above symptoms.

Between the attack of influenza and the lethargy during pregnancy she was perfectly well. She presents a parkinsonian attitude, facies and gait. The right arm and leg are hemiparetic and hypertonic, with increased deep reflexes and hemitremor of the paralysis agitans type, but without Babinski's sign. The left arm and leg are slightly hypertonic but not paretic. She is obese and has gained 80 pounds, her present weight being 235 pounds. She has polyuria, polydipsia and a large appetite. She is always drowsy, and there is mental apathy. The pupils are large, unequal in size and irregular; the light reaction is greatly impaired, the convergence contraction much better. At one time the pupils were of the Argyll Robertson type; of late the light reaction has improved. There is no defect in the visual fields. Lately she has spells of involuntary crying. The sugar tolerance is definitely lowered. The blood and spinal fluid Wassermann reactions are negative.

Case 2.—A man aged 30 who, three years after a mild attack of influenza in 1919, in which he was lethargic, began to develop the typical parkinsonian picture without tremor. The long interval of apparent normality is of interest.

Case 3.—A woman aged 25, also three years after a mild attack of encephalitis, began to develop a typical parkinsonian syndrome with slight right-handed tremor, the three year interval being free of symptoms. Immediately preceding the onset, the patient received a severe mental shock, to which her present condition is attributed by the family; perhaps this shock precipitated the symptoms.

Case 4.—A girl aged 4, who is unable to stand or walk, the legs being markedly ataxic and atrophic. The reflexes are exaggerated and the plantar responses flexor in type. The upper extremities are also ataxic and are held usually abducted with the hands clasped. The bladder is without voluntary control. The facial expression is idiotic; there is constant gnashing of teeth because of bilateral masseter spasm, and much drooling of saliva. The child is unable to talk. There is a tendency to internal strabismus. The right lower extremity is constantly being thrown about in gross purposeless movements, associated with much snorting and marked irregularity of respiratory rate and rhythm. In the ninth month of the gestation period, the mother had had encephalitis with much drowsiness. The child was born ten days before the expected time with no difficulty and not asphyxiated. She has had no convulsions. The child learned to walk and talk in normal time and at 16 months was able to say such words as "pretty thing" and to walk two blocks by holding on to the coach. At 18 months she began to retrogress, and in three months had reached the present state. It is presumed that the child had encephalitis in utero during the mother's attack and that a period of normality of eighteen months elapsed, such as we see in adults, before the development of the sequelae.

DISCUSSION

Dr. Alfred J. Ostheimer: I am much interested in Dr. Ornsteen's cases, on account of the length of time between these recrudescences (these lightings up of the old condition by some new infection or by the strain of pregnancy hitting, as it were, the locus minoris resistentiae) and the original acute attack. It may be that in my work in the U. S. Veteran's Bureau I am particularly interested in this condition because scientifically it brings out the fact that the original infection of ex-service men, which might have been so slight as to

have been overlooked, may have occurred in service and then it becomes possible to connect the sequelae with the service. Therefore, from the standpoint of professional opinion, it is a very great aid in bringing about justice to the ex-service man.

DR. W. G. SPILLER: Clinical recovery does not necessarily mean pathologic recovery. Schaller and Oliver have reported a case of chronic encephalitis extending over fourteen months and followed by necropsy. Some cases of encephalitis assume a chronic type, possibly with remissions. We may not conclude always, because the patient seems clinically well of encephalitis, that all pathologic changes have disappeared. It is possible that some patients carry inflammatory lesions in their brain for one or two years, or even longer, and it is not necessary to believe that the organism persists in the tissues. Cases are reported where symptoms have recurred after a considerable time following what was apparent recovery from encephalitis.

DR. F. X. DERCUM: The term influenza in these cases ought not to be confused with the original disease itself, namely encephalitis. There has been a tendency at times, I think, to confuse the early symptoms of encephalitis with those of influenza and again to correlate the two affections in such a way as to make encephalitis appear as a sequel of influenza. This is something which the facts do not justify. We need only to recall the history of the appearance of encephalitis in Vienna in 1916. It is noteworthy that there had been no influenza in Vienna for a long time previously. I think Dr. Spiller's view is the philosophic and scientific one to take. These patients are not well when they have recovered from their early symptoms. An antitoxin is early developed which results in a relative immunity and partial recovery, but sooner or later they exhaust their defensive resources and the symptoms recur. The same thing is seen in general paralysis. A case is rested and fed and a remission ensues, but sooner or later there is a recurrence of the symptoms.

DR. A. M. ORNSTEEN: The infrequency of these manifestations before the epidemic of influenza in 1918 as compared with the frequency now, cannot but make us consider the probable causal relationship between the original epidemic and the many cases of these syndromes that we see today.

"NAMES AND THINGS IN PSYCHIATRY." CHARLES W. BURR, M.D.

This paper will be published in full elsewhere.

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## CHICAGO NEUROLOGIC SOCIETY

*Regular Meeting, March 15, 1923*

H. I. DAVIS, M.D., *President, in the Chair*

A CLINICAL CASE PRESENTING INTERESTING MENTAL PHENOMENA. DR. GEORGE W. HALL.

This report will be published elsewhere.

MYOPATHY AND AMYOTONIA IN THE SAME PATIENT. DR. ALBERT B. YUDELSON.

*History.*—K. M., a white American girl, aged 10, who was first examined in July, 1920, was born when her father was 34 and her mother 32. The father

had a severe attack of typhoid fever in 1905 but made a good recovery. The parents are both well and there is nothing of signficance in the ancestral history. The patient is the eighth child. The first child was born dead, ten days after the mother slipped and fell; the second, seventh and twelfth children are living and well; the third and fourth were born prematurely and lived only three days; the ninth child died with "spasms" at the age of 3½; the tenth pregnancy was with twins, one of which is alive and well, the other died of influenza; the twelfth and last pregnancy resulted in a miscarriage in the third month.

The patient was a bright healthy child and began to walk and talk at sixteen months. She had whooping cough at 2 and measles at 5 years. When 2½ years of age, it was noticed that she did not walk as well as formerly and dragged the left leg. After walking less than a block, or when running across the floor, she would "flop down" to a sitting position; she did not fall, but just sat down suddenly. In getting up from the floor, she "stood on all fours" before balancing herself on her feet. The condition has gradually been getting worse; she has progressively walked less and fallen more often. Her hands and arms twitch and she frequently drops things. She is bright, holds her own with the other children, has ridden to school for the past two years and is now in the third grade. She can sing, read, write and sew.

*Examination.*—Development is asymmetrical but she is moderately well nourished, of good color, 4 feet 1½ inches (125.75 cm.) tall and weighs 51 pounds (23 kg.). The left side of the thorax appears smaller than the right; there is a scoliosis with convexity to the right and a moderate kyphosis of the middle third of the dorsal spine. The scapulas are winged; the left shoulder droops and the left arm appears correspondingly longer than the right when the patient stands erect.

The musculature in general is flabby and very deficient in tone, especially on the left side, and there is corresponding weakness. With the dynamometer the left hand registers 22, the right 26; the left foot registered 3, the right 5. This indicates marked weakness in the lower extremities. The neck muscles are the firmest and strongest in the body. There is a coarse tremor of the hands, which is increased on intention, and myoclonic movements are observed in the shoulder and gluteal muscles. There is no fibrillary twitching.

The arms can be raised above the head in full extension and adduction, abduction, flexion and extension of the shoulders are free and full. Flexion is good at the elbows, wrists and fingers; the thenar and hypothenar eminences are normal; pronation and supination are normal, though slower on the left than the right. The flexors generally are stronger than the extensors. With her hands the patient performs all purposive movements well except that they are slow, feeble and tremulous. Writing shows waves in the upstrokes.

Hypotonicity is extreme and much more marked in the lower than in the upper extremities; the trunk can be flexed on the thighs so that the head lies between the legs (closed jack-knife position). The knees also can be flexed with the hip abducted so that the feet are placed on the pubes. There is a tendency to club feet on both sides and recently a definite talipes equinovarus on the left; there are no contractures, localized atrophies, hypertrophy or pseudo-hypertrophy. Flexion and extension at the hips are absent; abduction and adduction are entirely absent in the left and nearly so in the right hip when the limbs are extended. When the knees and hips are flexed there is moderate power of adduction, better on the right. Dorsiflexion of the ankles is slow and weak but movement of the toes is normal.

In rising from a reclining position, the patient rolls toward the right, supporting herself on the elbow and pushing it upward so as to raise the right shoulder; then with a jerk of the left shoulder she throws the left hand across the trunk to the floor on the opposite side. The palm of the right hand is firmly planted on the floor by extending the right elbow; the trunk is gradually and with difficulty raised to the sitting position and the left arm is slowly withdrawn to its side. She then bends forward, takes hold of the legs just above the ankles and places the feet at the crotch so that the heels touch the buttocks. She throws her hands forward and to the right and stands on "all fours"; she then places her left hand on the left knee and, with a jerk, the right hand on the right knee and climbs up herself, jerking the head backward, the arms forward and the left leg outward to stand with a broad base.

The gait is broad-based and waddly. She looks downward and swings her arms as she steps, as though the arms assist in walking. The entire sole strikes the ground. The gait is like that of one walking on stilts; the trunk sways from side to side and the shoulders act as propellers. She walks unaided for about 30 to 40 feet. She drops to a sitting position without assistance. Walking is more difficult in cold or hot weather and in the later hours of the day. On retiring, the mother has to lift the patient's legs into bed and place them in extension. When a limb is lifted and released, it falls entirely without tonus.

The face is somewhat asymmetrical, but there is no facial palsy. The muscles of mastication are intact and deglutition is normal. The pupils are equal, regular, active to light and in accommodation. The left external rectus is paretic and there is a nystagmoid movement on inward excursion of that eye. When an object is placed directly in front of the left eye, the right eye ball rolls inward; there is no diplopia. The fundi are normal. Vision, hearing, smell and taste are normal. The tongue protrudes and opposes well, without deviation or tremor. Speech is distinct and of even tone; the voice is low. The teeth and tonsils are in good condition.

The superficial reflexes are normal and equal on the two sides. The deep reflexes in the upper extremities are normal and equal; the jaw jerk is present; the knee and Achilles jerks are absent. Muscle and joint sense are normal in the upper extremities and apparently also in the lower. The vibration sense in the lower extremities is faulty. There is no ataxia of station (Romberg test). Sensation in all phases is not impaired except in the legs where appreciation of cold is diminished.

Electrical tests show marked reduction in the reaction to both currents, especially in the legs, more so in the left; there is no reaction of degeneration. The facial muscles and those of the neck react promptly to galvanism and slowly to a faradic current of moderate strength. In the lower extremities a strong faradic current is borne without flinching.

The hair is coarse and dry, the skin soft and perspiration is scant. The legs are cyanotic and cold, and the integument is thick and tense. The nails are apparently normal. Sores heal very slowly and leave brown pigmentation.

*Comment.*—This case is a combination of myopathy with amyotonia, the latter predominating. That the onset was after birth is certain. She walked very well for more than a year. She was two and a half years old, when she was noticed to be limping, just after a severe attack of whooping cough. The symptoms indicative of amyotonia are: apathetic facies without paralysis; extreme hypotonia at all joints except wrists and ankles; winged scapulas; involvement of lower extremities; ability to perform normal purposive move-

ments, though feebly. There are no paralysis, atrophy, reaction of degeneration nor muscular twitching. The myopathy is indicated by: gradual onset after learning to walk; myoclonic movements; the gait; the manner of rising from the floor; club feet; and vasomotor changes in the legs.

The mother's obstetrical history should be considered as an etiologic factor. There is certainly marked reproductive disability. The first miscarriage may be said to have been accidental. All the other obstetrical mishaps occurred after the father had an attack of typhoid fever. Guillain observed three cases of myopathy following typhoid fever, but there is no case on record to show that the disease may be due to typhoid fever in either parent.

DISCUSSION

DR. JAMES C. GILL: Was the left external rectus paralyzed? Did the eye always remain turned in?

DR. YUDELSON: Under ordinary conditions the eye remains turned in, but it can turn out. It does not go beyond the median line except with great effort, and then the nystagmoid movements occur. I consider this a paresis of the external rectus.

DR. GILL: This is an interesting case, but I see no reason for classifying it as amyotonia congenita. It closely resembles the infantile myopathies commonly observed. With our present knowledge it seems to me confusing to combine these two classifications. I can see no difference between the description given by Dr. Yudelson and many myopathies. They do not all correspond to a type; some are rapid while others are slow in their progress and we meet all grades of this group of disorders.

DR. YUDELSON: The title chosen was given to avoid applying the name amyotonia congenita, and yet to show that many of the symptoms of both disorders may occur in one case. The symptoms in this case are those of a myopathy; hypotonia is also marked, though, as the history indicates, this case is not one of amyotonia congenita.

## THE FACTOR OF DETERIORATION IN CHILDREN SHOWING BEHAVIOR DIFFICULTIES FOLLOWING EPIDEMIC ENCEPHALITIS. DR. MANDEL SHERMAN and BERT I. BEVERLY (by invitation).

This report will be published in full in a later issue of the ARCHIVES.

# Book Reviews

CONCERNING PSYCHANALYSIS. Introductory presentation by RUDOLF ALLERS in Vienna with following discussion in the Society for Applied Psychopathology and Psychology in Vienna. (Summer Semester, 1920.) Edited by Prof. Dr. med. ERWIN STRANSKY, first presiding officer, and Dr. med. et jur. BERNHARD DATTNER, first secretary. No. 16 of Contributions in Neurology, Psychiatry, Psychology, and Their Allied Fields; supplements to the Monatschrift für Psychiatrie und Neurologie. Price, 40 marks. Pp. 119. Berlin: S. Karger, 1922.

We deal here with an unusual contribution, a criticism of psychanalysis (45 pages) by the neurophysiologist and psychologist Rudolf Allers, and about seventy-five pages of discussion by fourteen members of the society. It is a remarkable exhibit of the capacity of presentation, and the acumen and alertness of the speakers of a group made up of critics, friends and neutrals among Vienna psychologists and psychopathologists. The chief interest of the book lies in this fact that psychanalysis is here discussed from various widely divergent points of view including orthodox psychanalysis, academic clinical psychiatry, and phenomenologic psychology. A full review was therefore deemed desirable and essential, but proved decidedly difficult. An attempt was made to single out the special topics touched in the discussion so as to get into the smallest space and with maximal fairness a summary of the various opinions. Yet the reviewers fear that perhaps nothing but a perusal of the original could give a fair idea.

Allers and Schilder and most of the speakers use or refer to a cut-and-dried logic and formula very different from the psychodynamic and pragmatic formulations on this side of the Atlantic. They measure the product of Freud's life work by the criteria of another system of thought, instead of bringing both systems closer to the fundamentals. It might look like an unfair self-sufficiency to claim that there is a superabundance of chaff in such a procedure; but it certainly would be wiser to make a review of the whole phenomenologic and modern epistemologic approach to clear the atmosphere before taking up an inevitably complex problem like psychanalysis with an alien system of logic; provided, of course, that one feels that enough would come from such a task. The influence of Husserl makes itself strangely felt in German writings, and yet there is very little recognition in Anglo-Saxon philosophic and psychologic literature of any acceptance and use of this line of thought. The spirit of William James and John Dewey and the formulations of psychobiology follow essentially different lines with far more respect for pragmatic fundamentals. The psychiatric applications of Husserl's ideas are to be found in Jaspers. Too much of the discussion is an attempt to measure Freud with the rules of the special type of game. By eliminating the application of Freudian theory in treatment, the discussion eliminates the essentials of method and the source of most of the data, and thereby it loses its natural interest. Allers, on purpose, keeps his discussion on a definitely abstract level—to our minds unfortunately so because the whole is so very empirical and conjectural at the same time.

Allers limits the discussion to psychanalysis as a theory and method of research, shutting out the therapeutic aspect, as its results might not be any

proof of the theory. Since there is no concise and complete systematic presentation of the doctrine, Allers offers his own formulation of the theory.

He sees in psychanalysis: (1) a method of investigation to recognize mental connections; (2) a theoretical conception of the nature of the soul-life of man; (3) a therapeutic procedure (not to be discussed); and (4) a claim of giving fundamental explanations of all possible domains of human life—the science of religion and art, philosophy, pedagogy, sociology, and ethnology. He does not depict it in its historical evolution, but as a finished claim or theory of psychologic organization as found in Freud's writings. He gives a very full and lucid outline of his conception of the theoretical foundation of psychanalysis. This outline is rather cleverly formulated to arouse a host of questions, factual and theoretical. But Allers proceeds directly to the discussion of *psychanalysis* as *method,* which is essentially that of free associations (reporting immediately every rising thought, without expurgations, critique, or shame), the watching for any gaps, and evidences of resistance with the light it throws on the charge of affect and the importance of the topic and the actual causal and intelligible connections. Allers refers to the assumption of "typical symbolizations" and "typical contents" of the unconscious existing in all human beings (such as the infantile sexuality, the incest problem, etc.). The unconscious is made up of phylogenetically and ontogenetically old material; its thinking is archaic; it realizes itself in pictures, not in words or thoughts; it keeps its affects and therewith its dynamic potency in the face of the barrier of censorship against entrance into consciousness. When the previously unconscious material becomes conscious, it is usually, but not always, recognized as the person's own.

Psychanalysis claims to be an empirical science, Allers continues. It postulates a strict causal determinism (in contrast to Bergson's assumption of complete or partial freedom); psychanalysis is interested largely in causal explanation, not in the phenomenologic accounting (so strongly emphasized by the followers of Husserl, Jaspers, etc.). The theory works with energetic concepts, and assigns a rationalistic nature with reasons and concepts and thinking even, to the unconscious.

This factual part of Allers' address is not specifically challenged in the discussion; but more so his excluding the practical experience.

While admitting that psychanalysis has brought out a number of valuable discoveries, Allers turns from this objective account to his criticism of *the method* employed. He claims that he need not go to the trouble of actually employing the psychanalytic method for the control of the facts if he can show that the method, for any reasons whatsoever, either is bound to furnish certain special results or is never able to justify certain others. Correct results might be obtained, not because of; but in spite of, the psychanalytic technic. Therapeutic results, for instance, should not be taken as indubitable proof of the soundness of a method or theory.

The method is that of free association, the fundamental rule of communicating every arousal even if disagreeable or apparently irrelevant. Where gaps occur or the flow stops, the analyzer and the analyzand together have to overcome the resistance, and thereby they will bring out significant material from the unconscious. Allers sees in this a fatal petitio principii (p. 17). The mere fact of interruption of the free flow does not prove the existence of resistance and repression, unless other facts can be adduced as proof. In reality the hypothesis of repression anteceded the method of free association. It originated during the stage of the cathartic procedure. Neither the claim

of a resistance in the delay of the flow of association nor the causal significance of what is brought out by the effort of filling the break or gap is self-evident, and the conviction of its importance appears smuggled in by the introduction of the *concept of determination* which has at least four roots: it may point to a logical connection by sense or meaning, or to an associative relation of coexistence with or without relation by sense, or it may hang together emotionally, or it may be causal. Does the presence of symbols indicate causal relations? There may be a relation by meaning, but if an unknown quantity in an equation is designated by $x$, or if children use a piece of wood as a doll, we cannot say that the unknown *causes* the $x$, or the doll the piece of wood. The assumption of resistance and of a causal relation should not be assumed to exist without proof, merely on ground of the theory; and the theory cannot be properly based on such an assumption—hence a vicious circle. Further, the fact that "free association" is after all starting from components of a dream, or even from actual gaps in the dream, and has analysis as its goal, makes the association far from free. Moreover, there is no real end to the chain; each chain should properly include the totality of the psyche—correctly enough, but to the discomfiture of a theory of causation: each phenomenon would have the indivisible whole as its cause, and there would not be any distinctive difference in the causal importance of the different phenomena. The string of association is considered sufficient under the criteria of plausibility, of convergence upon a central point, and, when practicable, of the acceptance by the analyzand (the person analyzed). The analysis is sufficient if it gives a plausible picture of the latent thoughts, and this is based on the assumptions that a dream *does* represent an intelligible nexus of latent thoughts—which is a third petitio principii. Historically the theory arose in this way: the disappearance of the symptoms seemed to justify the conclusion that the disclosed material was causally effective and also determined the sense. "Can this be applied to the dream? Does the dream element disappear when the unconscious elements represented by it become conscious? There can be no disappearance because it is no longer present." (This passage is a fair illustration of the sophistic method of Allers.)

Allers can therefore sum up his logical argument as follows (p. 21): The claim that the method leads to the conclusion and inferences of psychanalysis rests on three vicious circles: that of the resistance, that of the causal determination, and that of the sense. It presupposes the whole of the theory which it claims to prove in each of its parts. The facts are: the strings of associations; and the occurrence of gaps. Everything else is interpretation resting on the theory to be proved. Yet the facts resolve themselves to nothing but this: Sometimes one associates and sometimes one does not—and "this finishes psychanalysis methodically." But there are other very startling aspects which Allers does not want to leave undiscussed.

The so-called laws of dream formation are merely laws of possible connection by sense, but not of causation. They largely coincide with the laws of association. Association by contrast may lead us to think of "secret" in a dream where there appear many persons; the latent element "secret" does not prove that the secret is the cause of the specially great number of dramatis personae. The association by contrast might very well have a root deeper than that of the meaning or sense of words; we know something like it in the phenomena of the negative after-image and in the phenomena of contrast. Allers admits, however, his reluctance in using physiologic analogies for the elucidation of psychologic facts.

The occurrence of sexual and infantile material in the chains of association need not surprise one, since in the mental life everything somehow is connected with everything else, but by no means necessarily causally connected.

Allers claims justly that as long as psychanalysis calls itself an empirical science, it should use controls. The invention of dreams seems to have been tried by Schroetter, but inadequately. Allers himself recommends the exposing of a picture and treating the impression as a dream with subsequent analysis—actually with very much the same result as with dreams, bringing out incestuous complexes, etc. Allers clearly is not inclined to look upon unconscious determiners as causes. He attributes the neglect of controls to the fact that the analytical conclusions were not obtained by the analytic method, but rather the method from the conclusions or intuitions.

He next turns against the interpretations and their (pathographic) application to dead personages in whom control is excluded. Not only the authors whom Freud calls irresponsible, but Freud himself indulges in the interpretation of "typical symbols." As to the sexual orientation of the interpretation, Allers admits that ethnology and folk-lore and ceremonials show that sexual associations do exist and are frequent, but not that they must be so of necessity. He quotes their occurrence in some ancient dream interpretations in an old Talmud tract. The generalization that hallucinations and delusions must be related to sex complexes he attributes to the diallelon (definition in a circle) of determination. With the discovery and appeal to "the unconscious yes" and the claim that there is no "unconscious no" the analyzer can always overrule the analyzand.

From the dissection and disposal of the "method," Allers passes to the discussion of the *concept of the unconscious* (p. 24). Disregarding those who object to the term, he accepts as recognized even outside of psychanalysis the concept of an unconscious and the terms "unconscious mental life" and "unconscious thinking"—as a description of a certain type of fact, or as an hypothetical formula, a consideration of "as if" there were such a thing. He does, however, question some points concerning the special structure and mode of functioning assigned to the unconscious by psychanalysis. He thinks little of the "metapsychologic" claim that the unconscious contains only concepts or images of things, whereas the conscious adds word concepts. This does not do justice to the phenomenology, i. e., the facts of consciousness as observed. We are supposed to assume that the unconscious contains what is repressed and unfit for, if not incapable of, consciousness, which has, however, a tendency to become conscious, either disfigured by the censorship or in its true form when the censorship is removed—in the cathartic procedure by hypnosis, or in free association through a force overcoming the resistance. But what is this force which is assumed to overcome the resistance? There evidently is another way, different from the overpowering of the censorship. Freud assumes for mental life something like the pattern of a reflex apparatus. The stimulus passes through several strata: a perceptive system, then memory systems, next the unconscious, the foreconscious, finally the conscious and the transformation into a motor act. Allers objects to the assumption of a close neuropsychologic parallelism, and the substitution of parts of the two systems for each other, and such expressions as the repression of old established association paths.

Between the unconscious and conscious the censorship is supposed to dominate, with selection and repression. If, however, the stimulus is regressive, from the conscious to the unconscious toward the perceptive spheres, there is

no need of overcoming the censorship (p. 26). The unconscious material then presents itself in the form of hallucinated memories. The process is the same as in remembering, in the search for a forgotten word. It is true, no explanation is offered as to how the images of the perceptive sphere reach consciousness. Allers sees in this a gap in the phenomenologic consideration, but one not limited to the psychanalysts. If remembering is regression through several strata into the unconscious, one should expect that the memory too would rise primarily as hallucination or image. If one uses the expression hallucinatory, one evidently introduces a fundamental distinction between concept and percept—evidently a problem for the neglected phenomenology. In trying to remember the andante of the Fifth Symphony, one experiences what William James called an active gap. Allers notes a sense of what is wanted, over and outside of the various trials, until fragments or the whole memory comes up with a feeling that what is wanted is found. Similarly that which rises as image is not a representation of the non-perceptual idea in a conceptual form; one gropes for merely superficial features, because one finds oneself "incapable of holding on to the non-perceptual thought." As one of the many possible forms of remembering he mentions how Grillparzer, trying to remember a quarrel he had seen, recast it in terms of a chess game. There is no fixed rule of regression working only with the fact-concept or thing-concept and the word-concept.

Allers makes it appear as if psychanalysis included in the unconscious the original drives, that which is repressed and incapable of consciousness, and probably also that which remains at any given moment as latent knowledge and latent "Einstellung" or set. It is only out of the unconscious that we can understand character-traits, peculiarities of the conduct of life and scientific and artistic productions.

One cannot help feeling that Allers takes us into a circus ring in which he rides the horse of a very elaborate and pedantic psychologic analysis, clad in the trappings of the psychologic vocabulary of detail observation similar to that of the Külpe or other introspectionist schools. Thus he suggests the working of the goal, the Aufgabe, where affects, but not contents, rise from the unconscious to influence the conscious.

Allers now (p. 30) turns to a second important part of the psychanalytic doctrine, that of *sexuality*, which is contrasted with the ego-tendencies. The latter have received but little attention except perhaps in Freud's article "Jenseits des Lustprincips." The modifications and expressions of sexuality figure as the causes of neuroses, psychoses, and normal phenomena. Libido, and that the libido of sexual nature, is made to include all psychic energy, or at least all that which serves the realization of the pleasure principle. Allers wants to call the pleasure derived from one's own body autohedonic and to distinguish between sexual and asexual tendencies. Similarity of the expressions should not be made to figure as identity. Thus a resemblance of religious ecstasy and of expressions of sexual experience does not prove that religious ecstasy is of sexual nature. Nor is sexual love *merely* sexual. The erotic component is only one of the most peripheral contributions of the central love act.

These fragmentary considerations concerning the concepts of the unconscious and of sexuality may not constitute as fundamental objections as were raised against the method. The method used and the results appear incompatible to Allers. Psychanalysis works with a quantitative consideration of mental life, and he objects seriously to the psycho-energetic treatment of the

emotional phenomena, the concept of the "Affectbetrag" and of entropy, etc. The sum of affects (quantities of affect) is transferred from one concept or topic to another; converted into physical phenomena, or disposed of by "abreaction" or by "conversion." These are notions naïvely borrowed from physics. Allers objects seriously to the application of the category of quantity to mental facts. One does, of course, speak of "more love," of "stronger feelings," "greater hatred," and even Kant speaks of intensities in the anticipation of perception, and Fechner of quantitatively equal increase of sensation. Allers claims that the concept of quantity holds only in the physical world. If hatred or love or a sensation is "stronger," it is not merely stronger but fundamentally and essentially different from a weaker one. In ordinary pragmatism the term may be tempting and permissible, and also the passing from the purely mental realm of immediate experience to the spatial-quantitative realm of external reality. On this point even academic psychology should not blunder any longer. He quotes Fritz Mauthner's condemnation of the use of the energy concept in the mental sphere and in memory which has no spatial relations and furnishes no unitary measure.

Psychanalysis and psychophysics fatally neglect the phenomenalistic orientation which treats mental life as an essentially indivisible whole, and involve themselves in all the errors of a dynamic association psychology. What can the energy be which is supposed to pass from sexual excitement into anxiety? How can one really speak of "sublimation?" The moral and social qualities of man are supposed to arise by sublimation from sexual energy or energy attached to sexuality. Psychanalysis assumes a primary repressive force. Where does it come from? Probably these difficulties have led to the opposition of the ego and sex tendencies. Allers sees in this not merely a lack of completion of the doctrine, but a deeply rooted fundamental flaw.

Thus Allers arrives at the following summary (p. 39): The psychanalytic theory cannot be derived from the empirical "psychanalytic" material unless one presupposes the theory. Three vicious circles appear: the petitio principii involved in the "resistance," in "determination," and the "intelligible connections." Hence it should not be supposed that the justification of the theory could be found in a definite set of fundamental facts; other categories would have to be found. Moreover, it follows that a control of the claims of psychanalysis with its own methods is absolutely devoid of purpose and sense. The system has inner contradictions and is based on an entirely untenable peculiar psycho-energetic fundamental conception. With all this, we recognize the fact that we owe to psychanalysis a great number of intuitions which strike one at once as new, valuable, and dependable, partly factual and partly in the way the problems are formulated.

Allers doubts that the categories of individual life can properly be applied to the group and totality as the psychanalysts do with regard to the social and ethnologic phenomena.

He next asks (p. 42) how such a structure could have been built up by a man of Freud's mental capacity, apparently based on logical mistakes, and how the doctrine could acquire such a following.

Psychanalysis arose at a time when the collapse of the natural history materialism and rationalism, with its tendency to "explain," began to lead over to the desire to "understand" connections (the passage from causalism to conditionalism). Symptoms called for an understanding out of the individual structure of the patient. But after all the attempt succumbed to a rationalistic tendency. Psychanalysis had started out to understand a living

entity, but ended in explanations of single moments. This fundamental tendency and the actual performance give rise to an antinomy which explains all the defects criticized. A fundamentally understanding procedure and an exquisitely rationalistic theory are incompatible. The procedure bent on understanding gives psychanalysis its intuitions and its therapeutic results, but not its explaining theory and method based on causality.

It seems convenient to present the discussion of Allers' lecture by arranging the various contributions according to the essential topics rather than by following the original sequence of the different speakers.

With regard to Allers' outline of the discussion, Schilder points out that, regarded from a historical point of view, psychanalysis started on empirical-inductive, not on speculative-deductive lines. It is doubtful whether a formal-logical approach is the right form of criticism for psychanalysis. He is convinced, however, after having discussed the more important topics of Allers, that psychanalysis stands well also the test of a formal logical critique. Fröschels contradicts Schilder's contention of a purely empirical science; science begins where special categories reign. Federn regrets that Allers did not include the therapeutic use of psychanalysis; it is not a question of the success of this therapy, but of the advantage of actual observation and research with patients, which brings out the psychic connections much more clearly than observation of normal people, or simple reading of psychanalytic literature, which is the case with Allers.

Pappenheim feels that the "imminent criticism" of Allers is not convincing. A refutation of the psychanalytic method in the way in which Allers approached this task is not possible. A discussion and criticism of the results of Freud's doctrine would have been more profitable than his methodologic examination. Roffenstein agrees with Allers that the theoretical foundation of the analytic method is insufficient; on the other hand he quotes Bleuler's account of the practical efficiency of the method in opening up facts which no other method would have brought out; and he warns against dismissing the method merely because the theoretical deductions and interpretations may as yet be inadequate.

The proof that the psychanalytic method as such leads to correct and dependable results is according to Federn threefold:

1. The occurrence of the same contents, in the child, in primitive man, and in the psychotic; this was not the basis of the psychanalytic discoveries, but constitutes its later confirmation. Roffenstein later denies that there exists a confirmation of the psychanalytic proposition by the psychology of primitive man. Freud, in his "Totem and Taboo," has not found the neurotic mechanisms in primitive man as independent parallel happenings, but he has reinterpreted the psychology of primitive man by his own method.

2. The feeling of the analyzed himself that a correct connection has been disclosed, with an experience of definite inner relief.

3. The change in symptoms in the analysis of a neurotic patient. For Pappenheim also the empirical fact of the mode of disappearance of symptoms is a more important point for the justification of the analytic procedure than any general "immanent" criticism.

With regard to the method of free association and the significance of resistance, Schilder discusses the fundamental importance of the fact that our flow of associations is dominated by what Ach called "determining tendencies"; these tendencies regulate our thinking as "latent determinations," of which the individual need not be conscious. This is one of the kind of facts, first discovered by Freud, which constitute the real foundation of psychanalysis, which

aims to formulate observations of a latent character as well as the obvious data. Gaps in the free flow of associations must therefore be of the greatest significance, and the formulations of censorship and resistance express this fact in an excellent way. Further, the method of free association is not meant to lead only to a knowledge of these underlying tendencies, but also to a knowledge of specific experiences from which a certain set of associations took its start. Federn charges Allers with a wrong view of the psychanalytic method. Nobody can deny "resistance" who has ever experienced it as analyst. Resistance (or we might add "the facts for which this term is used"), is not an assumption, but an observed experience, fully confirmed by Jung's association experiments. He gives a short abstract of an analysis showing the evidently strong affective outbursts after the overcoming of the resistance, which manifested itself in the case in various very suggestive ways. He concludes his remarks by expressing the wish that critics of psychanalysis may turn their attention not always to the basis of the method, but to those results of the method which are still uncertain, questions which he feels can only be solved by systematic psychanalytic work, and not by theoretical negation. Pappenheim points out that the existence of the resistance is not assumed merely from the formation of a gap in the sequence of free association, as Allers had contended, but that there are a number of other phenomena which indicate the resistance, e. g., mimic movements, which repeat themselves sometimes in a surprising way when the same topic is touched. He quotes Bleuler, who maintains that the actual blockings are only "a small and quite dispensable part of the foundations of our conclusions." According to Hitschmann, only he can understand that a gap in the flow of associations indicates a resistance who has actually seen it in statu nascendi in the patient.

The question of the causal significance of the material gained by psychanalysis is discussed by Schilder in a very interesting, though not altogether convincing way; he points to the aim of a true psychanalysis to distinguish between "understandable connections" and causal connections in each individual case. His chief argument, however, seems to be that, after all, the original fact from which psychanalysis started is the posthypnotic suggestion, where the conscious "motif" and the undoubtedly causal "motif," such as, for instance, the hypnotic suggestion, can be clearly distinguished. (It must be remembered, however, that historically, the starting point of the psychanalytic doctrine was not posthypnotic suggestion, but the removal of amnesia, as practiced by Bernheim in Nancy. Freud says himself: "This astonishing and instructive experiment was my model.") Schilder also does not seem to do justice to the fact that Freud changed his attitude with regard to the causal significance of a psychic trauma. Freud, it is true, came to a new formulation on strictly empirical grounds, but this change is of vital importance with regard to the theory of psychic determination. Hitschmann states that psychanalysis does not maintain that every psychic content is strictly causal and in every case only psychically determined. What psychanalysis maintains is that in many cases psychic determination can be proved to a far greater extent than had been assumed before. Roffenstein, who discusses the problem of causal relationship at some length, lays stress on the fact that the form in which the causality concept appears in psychanalysis is that form in which it has appeared first in the history of human knowledge, and has become the paradigma of all later causality concepts, viz., the expression of affects, of instincts, of volitional energy (p. 73). Allers contradicts this argument in his conclusion (p. 107), because we experience in our will first the fact of

being directed toward the realization of an imagined situation and therewith presuppose the possible connection between cause and effect.

With regard to the question of an intelligible sense of the dream, Pappenheim contradicts strongly Allers' view that the logical justification to interrupt an analysis at a point where one finds a possibility of construing a sense in the associated material, should rest on a petitio principii. He feels that there is no better example of a logical induction than when we draw conclusions from the disappearance of a symptom as to its causal connections with other symptoms. Hitschmann wants to confess to Allers that not every dream can be interpreted, and that we cannot always be sure whether we deal with a symbol or not. On the other hand he affirms that the physician interrupts the chain of association whenever he finds a crucial point indicated by a series of convergent associations and when he has got the conviction of a cogent interpretation. He thus admits the enormous freedom of interpretation in the analyst.

Concerning the question whether the results were obtained by the method or by intuition, Federn contends that a man must be "blind to the ways of research," if he really believes that Freud could have found a single one of the results of his doctrine without the psychanalytic method. Hitschmann believes he has found a proof for his view that Freud has obtained his results inductively by the psychanalytic method and not intuitively as Allers affirmed, in the fact that Freud's results were far too improbable for an intuitive discovery. He accepts only the first idea, that the dream may have a sense, as intuitive, and also the first attempt to put symbols in the place of typically recurrent dream elements for which the dreamer did not bring forth further associations. Everything else was careful and laborious observation and reexamination. Roffenstein regards Allers' statement of a knowledge "despite" the method instead of "through" the method as an improbable hypothesis; a clear distinction between method and result is not possible in the face of the close interconnection of the method with the partial results continuously obtained and the verification by the same method by pupils of the most divergent mental constitutions. Whatever may have been achieved by intuition, the theory, just as in chemistry and physics, could not have been achieved entirely without the method.

The psycho-energetic viewpoint to which Allers takes objection, is defended by Schilder, who points out that we deal here with an obvious hypothesis, independent of the fundamental doctrines of psychanalysis. Neumann, who represents the philosophically oriented psychology and phenomenology, objects to the psychanalytic doctrine of "psycho-energetic transformation," e. g., the transformation of libido into anxiety, because among other reasons anxiety is an experience and experiences cannot be transformed, nor can they arise by transformation. It seems to him that the psychanalytic theory does not distinguish sufficiently two different concepts of quantity (or rather of intensity), the intensity of experiences and the intensities of psychic energies.

Hitschmann thinks that control experiments to the interpretation of dreams are impossible and valueless, without, however, making his point quite convincing. Roffenstein on the other hand, urges that control experiments on a large systematic basis are necessary, especially to determine whether psychic productions, not produced by the patient, would give a sense in the analysis. In this case then, one could of course not speak of causality. He describes such a control experiment of Bleuler, where an artificial dream did not yield a sense on interpretation. Poetzl (p. 91) draws attention to his own control

experiments, which proved the validity of Freud's dream analysis. Dattner, who discusses the dream experiments by Scrötter, also thinks that control experiments, especially for the symbol dreams and interpretations, would be a very welcome support.

Roffenstein discusses in some detail the concept of the "Unconscious." He finds in this concept two different inner contradictions: (1) The assertion of the unconscious as something totally different from consciousness, as "a second empire," is not in harmony with the empirical unity of the whole personality, which demands a feeling of memory and confirmation for all psychic contents. (2) The assumption that we should claim as criterion an immediate empathic understanding (einfühlbares Verstehen), as proposed by Schilder, with his appeal to Husserl's concept of intuition, is in conflict with the definition of the concept of the unconscious, which, as something totally different from consciousness, should not at all be immediately intelligible by the means of consciousness.

Schilder designates Allers' view as erroneous, that Freud sees everywhere only *sex*. Freud distinguishes between sex-instinct and ego tendencies, the concept of narcistic libido being a sort of intermediate stage. It is true that the ego tendencies have not yet been elaborated as thoroughly as the sex instincts. Hitschmann also contradicts Allers' statement that, according to Freud, every pleasure is sexual pleasure, and every unconscious impulse is fundamentally sexual; he designates this as a distortion of the psychanalytic view. He raises what seems to be an excellent point against Allers' reproach that psychanalysis had originally altogether neglected the ego tendencies. He regards it as a matter of course that as psychanalysis started from the study of the transference-neuroses, repression was postulated, and the existence of a repressing principle was taken for granted, and the attention turned to the repressed facts. He admits that the examination of the ego tendencies has not yet been completed. He repudiates "the polymorph-perverse baby," mentioned controversially by Allers; all that Freud said is: "It is instructive that the child can become so under the influence of seduction." Freud has concluded retrospectively from his analyses that there is a close connection, an identity between the early and the later unmistakable actions of the erogenous zones. Allers maintains against this, in his conclusion, that Freud does actually speak of a "polymorph-perverse baby" in a different place. Mattauschek contends that the numerous war experiences have convincingly disproved the exclusively sexual etiology of the neuroses. In order to obviate confusion, Roffenstein calls for an answer to the concrete question, not sufficiently heeded by psychanalysis: what is the distinction between sexual joy and sexual instinct on the one hand, and non-sexual joy and non-sexual instinct on the other—introspectively as well as objectively—if psychanalysis considers as inadequate all our former biologic, anatomic, physiologic, and psychologic points of distinction?

Two further topics, both intimately connected with each other, and of importance in any discussion on psychanalysis, but outside of Allers' original outline of the topics to be discussed, are raised by Fröschels, viz., the problem of suggestion in psychanalysis and the question whether catharsis alone can effect a cure. Fröschels maintains that it is not possible to cure a psychoneurotic patient by catharsis, by digging out, as it were, a pathogenic experience or psychogenic experiences, because too much of what happened after the pathogenic event has itself become later a psychoneurotic complex or part of a complex; the soul being always a unity, it is impossible to get

hold cathartically of a pathogenic experience unchanged and without leaving a residual. The psychanalytic cure necessarily includes suggestion. Roffenstein, who feels that the mechanism of the "father transference" alone does not settle the question of suggestion, also considers suggestion an important factor in psychanalysis, not only for the direction of the flow of associations, but also for the therapeutic success.

Hitschmann draws attention to the conception of transference, "one of the most important observations of analysis." He contends that Allers has unduly neglected this point and this is the reason why he (Allers) cannot understand how the resistance is overcome during an analytic cure, a result obtained by hypnosis in the cathartic cure.

Roffenstein brings a new point in the discussion, the problem whether dreams and neuroses are really only regressions, or whether they do not have a "prospective tendency" as the Swiss group and Adler maintain. He thinks that the latter view corresponds better with a biologic point of view, for it is unlikely that a reminiscence, in the sense of a phylogenetic and ontogenetic residual, can have such important effects.

Trebitsch raises a new point in the discussion. He finds the explanation of the gulf between psychanalysis and "school psychology" in the existence of two different types of mentality, according to the prevalence of affirmation or negation from early childhood. The negated type, such as the Jew, finds a refuge from the negation by the environment in a precocious eroticism, and becomes sensitized in a manner unintelligible to those who did not grow up under negation (i. e., the dominant race). The psychanalytic doctrine deals only with this specific disposition, and is not generally valid. Stransky regards this point as very noteworthy, but warns against final formulations, especially in view of the strongly racial composition of the stubborn Swiss group of psychanalysts.

As gains of permanent value and "unconditionally acceptable," Allers mentions in his conclusion:

1. A better appreciation of sexuality, especially infantile sexuality.
2. The recognition of personality as a unit.
3. The existence of different psychic layers and recognition of the mechanisms of repression, condensation, and displacement.
4. The recognition of symbolism, restricted to a non-causal relationship; and of
5. Sublimation, also with certain theoretical reservations.

Allers seems to agree in his conclusion with Neumann who sums up his point of view in his contribution to the discussion, that the discovered facts will remain, but "very little of the theoretical substructure." Though this seems to be an extreme statement of a critical attitude toward psychanalysis, the book certainly is stimulating along this line of criticism.

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DIE EPIDEMISCHE ENCEPHALITIS. Prof. Felix Stern, Physician-in-Chief of the University Clinic for Mental and Nervous Diseases, Göttingen. Paper. Price, $2.80. Pp. 228. Berlin, Julius Springer, 1922.

This volume is the thirtieth monograph published under the auspices of the *Zeitschrift für die gesamte Neurologie und Psychiatrie*. It aims to cover in detail our existent knowledge of epidemic encephalitis, regarded as a clinical and pathologic entity. This is no light task, since, as the author states in the preface, no other subject in neurology, not excluding the voluminous war literature, has offered so many problems of pathologic and etiologic interest as has the pandemic of encephalitis. In spite of the fact that the first adequate description of the "new disease" by Economo was no longer ago than 1917, Stern gives in an appended bibliography a list of 372 references, about a third of those collected by the recent Report of the English Ministry of Public Health. The monograph is based on a personal study of 105 clinical cases and nine post-mortem examinations, together with a general review of the literature.

The subject-matter is divided into seven main headings as follows: (1) Clinical aspects; (2) Pathologic anatomy; (3) Epidemiology; (4) Pathogenesis; (5) Genesis of the somnolence; (6) Differential diagnosis; (7) Therapy. The first of these topics is discussed in great detail, taking more than half of the book in its exposition. This is an admirable statement of the manifold forms in which the disease may manifest itself, with constant text references to the work of other men and their opinions. The pathologic anatomy is treated in much more summary fashion in the space of twelve pages. It is, however, a good résumé of our knowledge, emphasizing the slight macroscopic changes, the non-hemorrhagic character of the lesions, the perivascular infiltration and blood-vessel changes, the slight tendency to softening, the predilection for certain areas, and the residual changes in the nerve tissue. Considering the epidemiology, the author does not question the existence of encephalitis of similar character previous to the present outbreak but there is no evidence that it has ever attained such proportions; and certainly it has never before been adequately studied. Its relation to influenza is regarded as not yet definitely determined; it is pointed out that the time relation of the two diseases has been inconstant and that in many instances encephalitis has preceded or been prevalent coincidentally with influenza, rather than consistently following it. On the other hand, their occurrence often in close association demands recognition of the fact that there may be a more intimate relationship between them than is as yet demonstrable. This matter is discussed in some detail in the section on pathogenesis. The statement is made that pandemic grippe and epidemic encephalitis stand in an indirect relationship to each other; that the essential virus of encephalitis is a filterable poison (noxe) which is present in harmless form in the mouths of many individuals; that the activation of this harmless "noxe" may take place through the virus of grippe which may also be activated by other organisms, for example, pneumococci or streptococci. The claim of a diplostreptococcus, as originally suggested by Economo and von Weisner, and the researches of Loewe and Strauss, Levaditi, Harvier and others relative to a filterable virus as possible causative agents, are critically examined and without prejudice, and also without any very definite conclusions. The discussion of the genesis of the characteristic somnolence naturally offers no solution of that unique phenomenon, but is interesting reading, particularly through the attempt to show its relation to normal sleep on the one hand, and to various pathologic

disturbances of consciousness on the other. Stern does not share the skepticism of many clinicians and investigators that convalescent serum has not demonstrated its value. He is very definite in his statement that such serum used in the acute stage is distinctly beneficial and quotes certain personal cases to establish his contention. Treatment by this means he thinks should be recommended in preference to the various drugs and other means of relief which have been widely used.

In general the monograph is readable, comprehensive in its scope and will serve as a most useful epitome of progress in the study of a disease, many of the problems of which have hardly been formulated, much less solved. There is no index; a somewhat complete table of contents does not atone for this omission.

MULTIPLE SCLEROSIS (DISSEMINATED SCLEROSIS). An Investigation by the Association for Research in Nervous and Mental Diseases. Cloth. Price, $3.75. Pp. 241. New York, Paul B. Hoeber, 1923.

Again we are indebted to the Association for Research in Nervous and Mental Diseases for a valuable and handy monograph. (The Association's volume on lethargic encephalitis was reviewed in these ARCHIVES **7**:151, 1922.) In December, 1921, the Association devoted a two days' meeting to the subject of multiple sclerosis and this volume of some 240 pages is the result. It contains the substance of all of the papers presented and of the discussions—if the procedure of quizzing the author can be called a discussion. There were twenty papers by twenty-six authors. These papers were taken in hand by the editorial board (Drs. Dana, Jelliffe, Riley, Tilney and Timme), properly edited and arranged in the following groups:

I. General and Historical Considerations.
II. General and Special Symptomatology.
III. Differential Diagnosis, Course and Treatment.
IV. Pathology.

At the meeting, after a paper was presented there was no general discussion but the author was questioned ad libitum by members of the Association. Occasionally this almost amounted to scientific "grilling." In the volume, the interrogation follows each paper, in some instances occupying ten or twelve pages.

At the close of each group of papers, e. g. General and Special Symptomatology, the Commission, which is the jury of the Association, briefly gives its conclusions. Thus the reader has not only the benefit of the author's presentation but also of elaboration and defense of his thesis elicited by the quizzing and of the mature opinion of a selected body of competent neurologists.

While the contents in detail and manner of construction of this monograph are far from those of the textbook or ordinary systematic treatise, the entire subject is covered and some of the matter is scarcely to be found elsewhere.

The historical introduction by Dr. Walter Timme is brief but adequate. Statistical papers by Drs. Charles B. Davenport and Pearce Bailey present new and interesting matter on geographic distribution, race incidence and incidence in United States troops in the late war. General statistics of the disease relating to morbidity incidence, incidence of age, sex, nativity, occupation, civil status, etc., are presented by Dr. Israel S. Wechsler, his conclusions being based on a study of 1,970 records, 1,773 from the literature and

197 from New York hospitals. Dr. Charles L. Dana contributes a brief paper on Multiple Sclerosis and the Methods of Ecology, we believe the first consideration of this matter for medical men.

There follow about forty-six pages by different authors relating to general and special symptomatology with some twenty-eight pages of questions by the Commission and answers by the authors. It may be noted that this section contains the results of special serologic studies, work on the spinal fluid, the last word on bacteriology of multiple sclerosis and a presentation of the attitude of a psychanalyst (Dr. Jelliffe) on Emotional and Psychological Factors in Multiple Sclerosis.

The work on the bacteriology of the disease, by Dr. Oscar Teague under the direction of Dr. Frederick Tilney, although uncompleted, is especially important. It has been more extensive and painstaking than any similar investigation up to the present time and quite negatives some rather startling statements of other workers affirming a specific organism.

Regarding "the probability that certain action patterns resulting from unconscious psychologic repressions and determining certain disturbances in the vascular distribution which result in the plaque formation of multiple sclerosis," the conclusion of the Commission may be quoted. "At present the Commission feels that it must accept this proposal merely as a suggestion which, in the absence of confirmatory observations and further proof, has not yet been established on a sufficiently firm basis to determine its validity."

In the section on Pathology the paper by Dr. Hassin contains what are probably the best illustrations of the histology of multiple sclerosis yet published and Dr. Joshua H. Leiner presents the latest work on the axis cylinder in this disease. (The illustrations of these two papers are reproduced from these ARCHIVES **7**:589, 1922; and **7**:608, 1922.) The difficulties of correlating the location of the lesions with the symptoms in individual cases are well discussed by Dr. E. W. Taylor, with illustrative cases.

A classified bibliography of about 600 titles closes the volume. That there is no index is matter for regret.

THE CONSTITUTIONAL FACTORS IN DEMENTIA PRAECOX WITH PARTICULAR ATTENTION TO THE CIRCULATORY SYSTEM AND TO SOME OF THE ENDOCRINE GLANDS. By NOLAN D. C. LEWIS, M.D. Nervous and Mental Disease Monograph Series No. 35. Paper. Price $3 Net. Pp. 134 with illustrations. New York: Nervous and Mental Disease Publishing Company, 1923.

The object of this study was to discover a basic constitutional factor in dementia praecox. The author distinguishes sharply between the hebephrenic, catatonic, and paranoid forms and regards the last as outside the province of true dementia praecox. The material was selected from the records of 4,400 postmortem examinations made at St. Elizabeth's Hospital and, after those instances in which the diagnosis was not clear and those in which there was a question of associated organic brain disease were excluded, there remained 601 cases of undoubted hebephrenia or catatonia. The incidence of pulmonary tuberculosis was so high that it became necessary to separate the material into eight groups: white males with tuberculosis, colored males with tuberculosis, white females with tuberculosis, colored females with tuberculosis, white males without tuberculosis, colored males without tuberculosis, white females

without tuberculosis, and colored females without tuberculosis. The following table is of considerable interest and gives the average heart weight in grams in each of the eight divisions.

| Group | No. of Cases | Average Heart Weight |
|---|---|---|
| 1 | 315 | 262.4 |
| 2 | 73 | 261 |
| 3 | 34 | 240 |
| 4 | 45 | 221 |
| 5 | 88 | 277 |
| 6 | 17 | 303 |
| 7 | 10 | 222 |
| 8 | 19 | 250 |

The average for the entire 601 cases, which was 254.4 gm. stands in striking contrast to the cardiac weights in arteriosclerotic dementia (399 gm.), senile dementia (362 gm.), parenchymatous neurosyphilis (281 gm.), manic-depressive (361 gm.), mesoblastic cerebral syphilis (331 gm.), epilepsy (366 gm.), and paranoid state (395) gm.). It will be noted that general paralysis is the only brain disease in which the low dementia praecox average is approached.

The monograph includes excellent detailed reports of the necropsy findings in twenty-two cases which will repay careful perusal. The chief items of interest may be referred to the aplastic circulatory system and the disorders of the thyroid, adrenal and gonads, with occasional involvement of the pituitary and mammary glands. The heart muscle is originally insufficient and the lumen of the aorta universally small—barely large enough to admit the first finger. Furthermore, the cardiac muscle lacks the capacity to hypertrophy, even in the presence of a valvular lesion. Microscopically, there is a lessened tendency for connective tissue replacement. The aortic walls are small, thin, smooth, and over-elastic and, since the main branches of the aorta likewise show aplasia, the assumption is that this is an index of the condition of the entire circulatory system. This corresponds to the circulatory aspects of the so-called status thymolymphaticus syndrome. The prominence of tuberculosis is presumably favored by the lymphostasis which exists on the following basis: "In most instances of dementia praecox constitution there is an aplastic or small circulatory system, and the lymphatic system, in order to account for intercellular spaces, must be large and wide. Since the widening of the bed of any stream produces slowing of the current, we have here perfect predisposing possibilities for the growth and advance of the lesions of tuberculosis without resorting to theories concerning prolonged confinement and lowered resistance, which factors also feature in other mental disorders not so often involved with tuberculosis. . . . The bacillus probably enters the hylus of the lung and passes along the peribronchial lymph channels to the periphery, and on account of the more sluggish lymph stream in the apices here produces its classical picture." The endocrine glands, particularly the thyroid, adrenals and gonads, revealed more or less constant gross and histologic departures from the normal and the author feels that the aplasias, atrophies, scleroses, and patchy hyperplasias are independent of the age of the individual, the duration of the psychosis, or the incidence of associated physical diseases and concludes that "they have suffered in the course of the development of the personality so that their respective functions are subsequently, imperfectly and aberrantly performed."

Naturally, the attempt to correlate the circulatory and ductless gland defects with the psychopathology and mental symptoms of schizophrenia implies a

considerable amount of supposition and yet the theory advanced is not without certain logical merit. The developmental shortcomings interfere with adequate response to a complicated environment and the organism regresses to a vegetative level where circulatory and endocrine adjustment is feasible. This would explain the preponderance of dementia praecox at puberty. The precipitating stress may be physical, chemical, psychic or social, in various combinations or in pure culture.

A minimum evaluation of Lewis' work is that it is a valuable contribution to the pathology of dementia praecox, the least understood of all the psychoses; the only permissible criticism is that there is not sufficient evidence to believe that the connection between somatic deficiencies and the mental picture is so simple and direct.